Mohamed
10/073277

```
=> fil reg
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               2.10       2.10

FILE 'REGISTRY' ENTERED AT 15:19:27 ON 13 APR 2004
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DICTIONARY FILE UPDATES:  12 APR 2004  HIGHEST RN 674767-20-5

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> e lactoferrin/cn 4
NUMBER OF TERMS TO DISPLAY IS OUT OF RANGE
The total number of terms displayed in a single EXPAND command
must be in the range 5-25.

=> e lactoferrin/cn 5
E1            1     LACTOFERRICIN H/CN
E2            1     LACTOFERRICIN H (HUMAN)/CN
E3            0 --> LACTOFERRIN/CN
E4            1     LACTOFERRIN (BUFFALO PRECURSOR)/CN
E5            1     LACTOFERRIN (CAMEL STRAIN SOMALI LACTATING MAMMARY GLAND)/CN

=> e lactoferrin human type/cn 5
E1            1     LACTOFERRIN BINDING PROTEIN B (MORAXELLA CATARRHALIS STRAIN
                    4223 CLONE PLD1-8 GENE LBPB)/CN
E2            1     LACTOFERRIN BINDING PROTEIN B (MORAXELLA CATARRHALIS STRAIN
                    Q8 CLONE PLDW1 GENE LBPB)/CN
E3            0 --> LACTOFERRIN HUMAN TYPE/CN
E4            1     LACTOFERRIN PRECURSOR (HUMAN)/CN
E5            1     LACTOFERRIN RECEPTOR (HUMAN SMALL INTESTINE)/CN

=> e human type lactoferrin /cn 5
E1            1     HUMAN TYPE 1 INOSITOL 1,4,5-TRISPHOSPHATE RECEPTOR (HUMAN CE
                    LL LINE HL-60 CLONE 5T42, 81SB1, 6YBH1, 6Y, 416-11L AND R62
                    GENE INSP3RI)/CN
E2            1     HUMAN TYPE 3 INOSITOL 1,4,5-TRISPHOSPHATE RECEPTOR (HUMAN CE
                    LL LINE HT29 GENE ITPR3)/CN
E3            0 --> HUMAN TYPE LACTOFERRIN/CN
E4            1     HUMAN TYPE XVIII COLLAGEN (HUMAN CLONE P310E12 GENE COL18A1)
                    /CN
E5            1     HUMAN TYPE XVIII COLLAGEN (HUMAN GENE COL18A1)/CN

=> e lactotransferrin/cn 5
E1            1     LACTOTETRAOSYLCERAMIDE/CN
```

Searched by: Mary Hale 571-272-2507 REM 1D86

```
E2            1     LACTOTHAMNOLIC ACID/CN
E3            0 --> LACTOTRANSFERRIN/CN
E4            1     LACTOTRANSFERRIN (HUMAN CLONE MGC:13618 IMAGE:4251222)/CN
E5            1     LACTOTRANSFERRIN (HUMAN CLONE MGC:13619 IMAGE:4294752)/CN

=> e lactoglobulin/cn 5
E1            1     LACTOGENIC HORMONE, PLACENTAL/CN
E2            1     LACTOGENIC HORMONE-RELEASING FACTOR/CN
E3            0 --> LACTOGLOBULIN/CN
E4            1     LACTOGLOBULIN (HUMAN)/CN
E5            1     LACTOGLOBULIN, B-/CN

=> fil medl,hcapl,biosis,embase,jicst,wpids;s (?lactoferrin? or lactotransferrin?
or lactoglobulin) and (inflam? or swell? or edema) and (body fluid or albumin or
neutrophil or tumor necrosis factor alpha or tnf alpha)
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       1.68       3.78

FILE 'MEDLINE' ENTERED AT 15:22:02 ON 13 APR 2004

FILE 'HCAPLUS' ENTERED AT 15:22:02 ON 13 APR 2004
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FILE 'WPIDS' ENTERED AT 15:22:02 ON 13 APR 2004
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L1          372 FILE MEDLINE
L2          251 FILE HCAPLUS
L3          323 FILE BIOSIS
L4          347 FILE EMBASE
LEFT TRUNCATION IGNORED FOR '?LACTOFERRIN?' FOR FILE 'JICST-EPLUS'
L5           36 FILE JICST-EPLUS
L6           30 FILE WPIDS

TOTAL FOR ALL FILES
L7         1359 (?LACTOFERRIN? OR LACTOTRANSFERRIN? OR LACTOGLOBULIN) AND (INFLA
                M? OR SWELL? OR EDEMA) AND (BODY FLUID OR ALBUMIN OR NEUTROPHIL
                OR TUMOR NECROSIS FACTOR ALPHA OR TNF ALPHA)
Left truncation is not valid in the specified search field in the
specified file.  The term has been searched without left truncation.
Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID'
would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you
used a truncation symbol after a punctuation mark, the system may
interpret the truncation symbol as being at the beginning of a term.
Implied proximity is used in search fields indexed as single words,
for example, the Basic Index.


Searched by: Mary Hale 571-272-2507 REM 1D86
```

```
=>
=> s l7 and (treat? or therap? or pharm?)
L8          173 FILE MEDLINE
L9           79 FILE HCAPLUS
L10         102 FILE BIOSIS
L11         134 FILE EMBASE
L12           9 FILE JICST-EPLUS
L13          22 FILE WPIDS

TOTAL FOR ALL FILES
L14         519 L7 AND (TREAT? OR THERAP? OR PHARM?)

=> s l7 and (oral? or intraperitoneal or inject?)
L15          42 FILE MEDLINE
L16          38 FILE HCAPLUS
L17          41 FILE BIOSIS
L18          46 FILE EMBASE
L19          10 FILE JICST-EPLUS
L20           5 FILE WPIDS

TOTAL FOR ALL FILES
L21         182 L7 AND (ORAL? OR INTRAPERITONEAL OR INJECT?)

=> s l21 and (food or medicine)
L22           3 FILE MEDLINE
L23           5 FILE HCAPLUS
L24          15 FILE BIOSIS
L25           2 FILE EMBASE
L26           3 FILE JICST-EPLUS
L27           1 FILE WPIDS

TOTAL FOR ALL FILES
L28          29 L21 AND (FOOD OR MEDICINE)

=> s l7 and parental?
L29           0 FILE MEDLINE
L30           0 FILE HCAPLUS
L31           0 FILE BIOSIS
L32           0 FILE EMBASE
L33           0 FILE JICST-EPLUS
L34           0 FILE WPIDS

TOTAL FOR ALL FILES
L35           0 L7 AND PARENTAL?

=> s human? and l28
L36           3 FILE MEDLINE
L37           4 FILE HCAPLUS
L38          13 FILE BIOSIS
L39           2 FILE EMBASE
L40           1 FILE JICST-EPLUS
L41           1 FILE WPIDS

TOTAL FOR ALL FILES
L42          24 HUMAN? AND L28

=> dup rem l42
PROCESSING COMPLETED FOR L42
L43          19 DUP REM L42 (5 DUPLICATES REMOVED)

=> s l7 and ingest?
L44           8 FILE MEDLINE


Searched by: Mary Hale 571-272-2507 REM 1D86
```

```
L45           8 FILE HCAPLUS
L46          27 FILE BIOSIS
L47           8 FILE EMBASE
L48           0 FILE JICST-EPLUS
L49           0 FILE WPIDS

TOTAL FOR ALL FILES
L50          51 L7 AND INGEST?

=> s l50 not l42
L51           8 FILE MEDLINE
L52           8 FILE HCAPLUS
L53          26 FILE BIOSIS
L54           8 FILE EMBASE
L55           0 FILE JICST-EPLUS
L56           0 FILE WPIDS

TOTAL FOR ALL FILES
L57          50 L50 NOT L42

=> dup rem l57
PROCESSING COMPLETED FOR L57
L58          33 DUP REM L57 (17 DUPLICATES REMOVED)

=> d l43 1-19 ibib abs;d l58 1-33 ibib abs
```

L43 ANSWER 1 OF 19 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2003202217 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12720494
TITLE: The therapeutic potential of **lactoferrin**.
AUTHOR: Weinberg Eugene D
CORPORATE SOURCE: Department of Biology and Programme in Medical Sciences, Indiana University, Bloomington, Indiana, USA.. eweinber@indiana.edu
SOURCE: Expert opinion on investigational drugs, (2003 May) 12 (5) 841-51. Ref: 115
Journal code: 9434197. ISSN: 1354-3784.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20030501
Last Updated on STN: 20030815
Entered Medline: 20030814

AB **Lactoferrin** (Lf), a natural defence iron-binding protein, is present in exocrine secretions that are commonly exposed to normal flora: milk, tears, nasal exudate, saliva, bronchial mucus, gastrointestinal fluids, cervicovaginal mucus and seminal fluid. Additionally, Lf is produced in polymorphonuclear leukocytes and is deposited by these circulating cells in septic sites. A principal function of Lf is that of scavenging non-protein-bound iron in **body fluids** and **inflamed** areas so as to suppress free radical-mediated damage and decrease accessibility of the metal to invading bacterial, fungal and neoplastic cells. Adequate sources of bovine and recombinant **human** Lf are now available for development of commercial applications. Among the latter are use of Lf in **food** preservation, fish farming, infant milk formula and **oral** hygiene. Other readily accessible body compartments for Lf administration include skin, throat and small intestine. Further research is needed for

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possible medicinal use in colon and systemic tissues. Although Lf is a natural product and should be highly biocompatible, possible hazards have been documented.

L43 ANSWER 2 OF 19 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:184094 BIOSIS
DOCUMENT NUMBER: PREV200300184094
TITLE: Chronic **inflammation** around painless partially erupted third molars.
AUTHOR(S): Laine, Mikael; Venta, Irja; Hyrkas, Tapio; Ma, Jian; Konttinen, Yrjo T. [Reprint Author]
CORPORATE SOURCE: Biomedicum, 00029, PO Box 700, Helsinki, Finland yrjo.konttinen@helsinki.fi
SOURCE: Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontics, (March 2003) Vol. 95, No. 3, pp. 277-282. print.
ISSN: 1079-2104 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Apr 2003
Last Updated on STN: 9 Apr 2003

AB Objectives: We sought to assess the histologic host response in chronic, symptomless pericoronitis. Study design: Gingival mucosal (n=20) and dental follicle (n=20) samples were collected during extraction from patients with pericoronitis and clinically healthy control subjects. Antibodies-recognizing macrophages (CD68), natural killer cells (CD56), T cells (CD2), helper T cells (CD4), suppressor/cytotoxic T cells (CD8), and **neutrophils** (**lactoferrin**) were applied in a labelled streptavidin-biotin method by using a DAKO TechMate staining robot. Results: Macrophage was the most numerous kind of cell in pericoronitis, but CD2+ T lymphocytes, with a normal CD4/CD8 ratio, were also increased (P<.01). **Neutrophils** were not increased and did not show signs of activation. Dental follicles did not contain increased numbers of **inflammatory** cells. Conclusion: This type of pericoronitis is a chronic/smoldering, rather than an acute/purulent, infection. Because of the chronic and often symptomless nature of pericoronitis, various long-term sequelae may result, which may lead to the need for extraction.

L43 ANSWER 3 OF 19 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003398718 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12935535
TITLE: Immunohistochemical detection of sepsis-induced lung injury in **human** autopsy material.
AUTHOR: Tsokos Michael
CORPORATE SOURCE: Institute of Legal Medicine, University of Hamburg, Butenfeld 34, D-22529, Hamburg, Germany.. mtsokos@web.de
SOURCE: Legal medicine (Tokyo, Japan), (2003 Jun) 5 (2) 73-86. Ref: 70
Journal code: 100889186. ISSN: 1344-6223.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20030826
Last Updated on STN: 20031218
Entered Medline: 20031204

AB This review addresses our present-day knowledge on the role of different cellular adhesion molecules, cytokines and glycoproteins for the detection of sepsis-induced injury in the microvasculature of the **human**

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lung using immunohistochemistry. Through the induction and modulation of endothelial cell adhesion molecules, such as E-selectin (CD 62E), the vascular endothelium controls leukocyte extravasation into tissue. E-Selectin, not expressed by unstimulated endothelium, is activated by cytokines and initiates **neutrophil** recruitment in sepsis-induced lung injury. Since E-selectin is strongly expressed in the pulmonary microvasculature in sepsis-associated fatalities, the immunohistochemical detection of an intense expression of E-selectin in lung tissue is a valuable diagnostic tool in the forensic postmortem elucidation of death due to sepsis. VLA-4 (CD49d/CD29) is strongly expressed on intravascular, interstitial and intra-alveolar leukocytes in sepsis-associated fatalities, whereas in non-septic fatalities an irregular weak immunoreactivity can be observed on interstitial leukocytes and no positive immunohistochemical expression can be observed on intravascular or intra-alveolar leukocytes. ICAM-1 (CD54) is strongly expressed on endothelial cells of the pulmonary microvasculature and on pulmonary macrophages and lymphocytes in sepsis-associated fatalities. In contrast, an infrequent weak immunohistochemical reaction for ICAM-1 is found on pulmonary endothelium and on perivascular leukocytes in non-septic fatalities. The up-regulation of both cellular adhesion molecules can be considered as an useful immunohistochemical postmortem marker of sepsis. **Lactoferrin** (LF) is an iron-binding glycoprotein located in specific (secondary) granules of leukocytes and plays a central role in the host response to infectious stimuli in providing both bacteriostatic and bactericidal protection. There is a statistically significant association between an enhanced expression of LF on pulmonary leukocytes in sepsis-related fatalities in contrast to non-septic controls. The immunohistochemical detection of an enhanced expression of LF can contribute to the postmortem discrimination between sepsis and non-septic fatalities. Application of carbohydrate-specific lectins (ConA, UEA, GSA I, GSA II, MPA, PNA, Jac, WGA, MAA, LPA, SNA) on deparaffinated lung tissue sections from sepsis-associated fatalities and control cases results to some extent in different staining patterns of alveolar epithelial cells and subepithelial seromucous glands of the bronchi. Apart from differences in binding sites for alpha-mannose, N-acetyl-neuraminic acid and alpha-(2-6)-galactose (as detected by different expression for ConA, MAA and SNA), the main finding is that no binding sites for alpha-N-acetyl-galactosamine (as investigated by MPA immunoreactivity) can be detected on alveolar epithelial cells and mucous parts of subepithelial seromucous glands in sepsis cases in contrast to the presence of such binding sites in controls. Since most intracellular pathogens persist in macrophages and epithelial cells during infection, it is likely that these pathogens contribute to a continual deprivation or consumption, respectively, of glycoproteins physiologically secreted by alveolar epithelial and glandular cells at different time points and stages of infection and may, among other mechanisms, by reducing pathogen clearance amplify the **inflammatory** response. Vascular endothelial growth factor (VEGF), an angiogenic and chemotactic peptide, is abundantly expressed in normal lung tissue, especially in alveolar and bronchial epithelium, glandular cells of the bronchi, and activated alveolar macrophages. Pulmonary VEGF immunostaining differs in sepsis when compared to healthy individuals. In the latter a preponderant strong VEGF immunoreaction can be found on alveolar epithelium (predominately type II pneumocytes), bronchial epithelium and glandular cells of the bronchi and bronchioli, and activated alveolar macrophages. In contrast, in sepsis no VEGF immunopositivity can beivity can be observed on bronchial epithelium or glandular cells of the bronchi and bronchioli, and no or relatively sparse VEGF immunoreactivity is found on alveolar epithelial cells. The precise mechanisms of the decreased pulmonary VEGF expression in septic patients under conditions of intensive care **medicine** are not clear at present. During the complex cascade of excessive pro-**inflammatory** and anti-**inflammatory**

mediator release involved in the host's systemic **inflammatory** response in the development of sepsis-induced lung injury, VEGF expression may be suppressed in sepsis by a hitherto not identified agent or the interaction of different mediators of cellular **inflammation.** For the detection of sepsis-induced lung injury the aforementioned markers can be used sufficiently, e.g. to give immunohistochemical evidence of a previously undiagnosed sepsis and to confirm or rule out a presumed diagnosis of a sepsis-associated fatality. The employment of the presented immunohistochemical methods will be particularly helpful when macroscopical and routine histological autopsy findings in cases of suspected fatal sepsis are unspecific or unconvincing, respectively, and clinical data on the patient's previous history are not available. Referring to the forensic argumentation regarding causality on the subject of possibly fatal septic complications, e.g. in the sequel of diagnostic or therapeutic iatrogenic **injection** procedures or being relevant to pressure sore-associated fatalities, aetiopathogenetic conclusions can be optimized on the basis of the described micromorphological investigations.

L43 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2002:866794 HCAPLUS
DOCUMENT NUMBER: 137:346180
TITLE: **Lactoferrins** for inhibiting formation of **inflammatory** cytokines
INVENTOR(S): Yamaguchi, Makoto; Nakamura, Yoshitaka; Sasaki, Hajime; Takahashi, Takeshi
PATENT ASSIGNEE(S): Meiji Milk Products, Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002326950	A2	20021115	JP 2001-135521	20010502

PRIORITY APPLN. INFO.: JP 2001-135521 20010502

AB **Lactoferrins**, including recombinant **human** **lactoferrins** with amino acid sequence Gly-Arg-Arg-Arg-Arg at N-terminal, are claimed for inhibiting **inflammatory** cytokines, including **TNF**-α and using RAW264 cell line for bioassay of endocytosis, and heparin uptake. **Lactoferrins** can be given **orally** or in enteral nutrients as health **foods** for treatment of **inflammatory** diseases. In addition, the screening method of this kind of Lf is offered. The ended sight - the fact that which the cis is done controls **inflammation** characteristic sight Cain production was discovered at the time of ligand taking in experimenting which uses the cultured cell.

L43 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:616360 HCAPLUS
DOCUMENT NUMBER: 137:150231
TITLE: Alleviating **inflammation** symptoms by administering a composition containing **human**-type **lactoferrin**
INVENTOR(S): Yajima, Masako; Nakayama, Makiko; Tsukamoto, Yumi; Koide, Kaoru; Kuwata, Tamotsu; Yajima, Takaji
PATENT ASSIGNEE(S): Meiji Dairies Corporation, Japan
SOURCE: U.S. Pat. Appl. Publ., 13 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent

Searched by: Mary Hale 571-272-2507 REM 1D86

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002111295	A1	20020815	US 2002-73297	20020213
JP 2002241301	A2	20020828	JP 2001-38486	20010215

PRIORITY APPLN. INFO.: JP 2001-38486 A 20010215

AB The invention provides agents for alleviating symptoms resulting from **inflammation**, which have an activity to alleviate **inflammatory** symptoms caused by bacterial infection, particularly accumulation of **body fluid** such as bronchocavernous plasma exudation, ascites, etc., at the **inflammatory** site, or excessive increase of blood **neutrophils**; symptoms resulting from **inflammation** caused by bacterial infection, particularly accumulation of **body fluid** such as bronchocavernous plasma exudation ascites, etc., at the **inflammatory** site, or excessive increase of blood **neutrophils**, can be alleviated effectively by infesting or administering **orally** or parenterally a composition containing **human**-type **lactoferrin** as an effective component.

L43 ANSWER 6 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2001689981 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11737657
TITLE: **Lactoferrin**, amylase and mucin MUC5B and their relation to the **oral** microflora in hyposalivation of different origins.
AUTHOR: Almstahl A; Wikstrom M; Groenink J
CORPORATE SOURCE: Department of Oral Microbiology, Institute of Odontology, Goteborg University, Box 450, SE-405 30 Goteborg, Sweden.
SOURCE: Oral microbiology and immunology, (2001 Dec) 16 (6) 345-52. Journal code: 8707451. ISSN: 0902-0055.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Dental Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20011213
Last Updated on STN: 20020209
Entered Medline: 20020208

AB There are several reasons for hyposalivation, each affecting the salivary composition in different ways. The aim of this study was to analyze and compare **lactoferrin**, amylase and mucin MUC5B in stimulated whole saliva collected from subjects with hyposalivation of different origins and to relate the results to the presence of some microbial species associated with **oral** disorders. **Albumin** was determined as a marker of serum leakage. The characteristic feature for subjects with radiation-induced hyposalivation was a large increase in **lactoferrin**, probably due to leakage through **inflamed** mucosal tissues, while it was a high **albumin** content for the group with primary Sjogren's syndrome, probably due to disruption of the fragile mucosa. The saliva composition in subjects with hyposalivation of unknown origin or due to **medicines** was close to that in the healthy controls. All three hyposalivation groups tended to display a decrease in the concentrations of MUC5B and amylase. None of the microbial species analyzed (streptococci, mutans streptococci, Lactobacillus spp., Fusobacterium nucleatum, Prevotella intermedia/Prevotella nigrescens, Candida albicans, Staphylococcus aureus and enterics) correlated with concentration of MUC5B in saliva. The RT group, having the highest concentration of **lactoferrin**, had the

lowest median number of F. nucleatum and was the only group in which median number of P. intermedia/P. nigrescens was zero.

L43 ANSWER 7 OF 19 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:388054 BIOSIS
DOCUMENT NUMBER: PREV200100388054
TITLE: Tobacco smoking and **neutrophil** activity in patients with periodontal disease.
AUTHOR(S): Persson, Lena [Reprint author]; Bergstrom, Jan; Ito, Hiroshi; Gustafsson, Anders
CORPORATE SOURCE: Department of Periodontology, Karolinska Institutet, SE-141 04, Huddinge, Sweden
Lena.Persson@ofa.ki.se
SOURCE: Journal of Periodontology, (January, 2001) Vol. 72, No. 1, pp. 90-95. print.
CODEN: JOPRAJ. ISSN: 0022-3492.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Aug 2001
Last Updated on STN: 19 Feb 2002

AB Background: Tobacco smoking has considerable negative effects on periodontal health. The mechanisms behind these effects are incompletely understood but may be related to the host response. The aim of the present study was to investigate the influence of tobacco smoking on the gingival crevicular fluid (GCF) levels of elastase, **lactoferrin** (LF), alpha-1-antitrypsin (alpha-1-AT), and alpha-2-macroglobulin (alpha-2-MG) under periodontally diseased conditions. Methods: The study population included 15 smokers (5 women and 10 men) aged 34 to 69 years and 17 non-smokers (5 women and 12 men) aged 31 to 81 years. Clinical registration of gingival index (GI), plaque index (PI), probing depth, as well as sampling of GCF were made at 3 sites with severe lesions and 3 sites with moderate lesions in each individual. The elastase activity was measured with a chromogenic low molecular substrate and the LF, alpha-1-AT, and alpha-2-MG concentrations with ELISA. Results: The results showed that, with regard to severe lesions, smokers had a significantly lower concentration of alpha-2-MG as well as significantly lower total amounts of alpha-2-MG and alpha-1-AT than non-smokers. With regard to moderate lesions, smokers tended to exhibit a lower concentration of alpha-2-MG, but the difference was not statistically significant. Comparing moderate and severe lesions, smokers exhibited no gradual increase with disease severity in contrast to non-smokers, who showed significantly or almost significantly increased levels of LF and alpha-2-MG in severe as compared to moderate lesions. Conclusions: The present results indicate that the levels of alpha-2-MG and alpha-1-AT are suppressed in smokers with periodontitis, suggesting that smoking interferes with these protease inhibitors. This may be one mechanism by which smoking affects the **inflammatory** response.

L43 ANSWER 8 OF 19 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:317019 BIOSIS
DOCUMENT NUMBER: PREV200000317019
TITLE: Temporal patterns of mediator release during developing cutaneous late-phase reactions.
AUTHOR(S): Zweiman, B. [Reprint author]; Von Allmen, C.
CORPORATE SOURCE: University of Pennsylvania School of Medicine, 512 Johnson Pavilion, Philadelphia, PA, 19104, USA
SOURCE: Clinical and Experimental Allergy, (June, 2000) Vol. 30, No. 6, pp. 856-862. print.
ISSN: 0954-7894.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jul 2000

Searched by: Mary Hale 571-272-2507 REM 1D86

Last Updated on STN: 7 Jan 2002

AB Background Several **inflammatory** mediators have been found released in sites of cutaneous late phase reactions (LPR). However, the temporal pattern of their release during LPR development has not been characterized. Objective Determine hourly accumulation of mediator release in comparison with gross and **inflammatory** cell responses during developing LPR. Methods Skin chamber appended to sites of allergen and diluent control challenge with hourly collections. Then, study of exuding leucocytes in chamber bases. Results In the allergen-challenged sites, histamine release peaked in the first hour, then low level release over the next 5 h. **Lactoferrin** release from **neutrophils** started by the second hour, likely associated with released IL-8. Eosinophil cationic protein levels started increasing slightly later. The percentage of exuding leucocytes which were activated was significantly higher in the allergen challenge sites than in the control challenge sites Conclusions Both gross LPR and local **inflammatory** cell responses in the skin start soon after the immediate mast cell activation in IgE-mediated responses. Such **inflammatory** responses include leucocyte activation and mediator release.

L43 ANSWER 9 OF 19 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1997:274628 BIOSIS
DOCUMENT NUMBER: PREV199799566346
TITLE: Effect of a recombinant dimeric tumor necrosis factor receptor on **inflammatory** responses to intravenous endotoxin in normal **humans**.
AUTHOR(S): Van Der Poll, Tom; Coyle, Susette M.; Levi, Marcel; Jansen, Patty M.; Dentener, Mieke; Barbosa, Karen; Buurman, Wim A.; Hack, C. Erik; Ten Cate, Jan W.; Agosti, Jan M.; Lowry, Stephen F. [Reprint author]
CORPORATE SOURCE: UMDNJ-Robert Wood Johnson Med. Sch., One Robert Wood Johnson Place, CN-19, New Brunswick, NJ 08903, USA
SOURCE: Blood, (1997) Vol. 89, No. 10, pp. 3727-3734. CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jun 1997
Last Updated on STN: 24 Jun 1997

AB To determine the role of tumor necrosis factor (TNF) in lipopolysaccharide (LPS)-induced **inflammation**, 12 healthy subjects received an intravenous **injection** with LPS (2 ng/kg) preceded by infusion of either a recombinant **human** dimeric TNF receptor type II-IgG fusion protein (TNFR:Fc, 6 mg/m-2; n = 6) or vehicle (n = 6) from -30 minutes to directly before LPS **injection**. LPS elicited a transient increase in plasma TNF activity, peaking after 1.5 hours (219 +- 42 pg/mL; P lt .05). Infusion of TNFR:Fc completely neutralized endogenous TNF activity. LPS administration was associated with an early activation of fibrinolysis (plasma concentrations of tissue-type plasminogen activator, plasminogen activator activity, and plasmin-alpha-2-antiplasmin complexes), followed by inhibition (plasma plasminogen activator inhibitor type I), changes that were completely prevented by TNFR:Fc. By contrast, TNFR:Fc did not influence LPS-induced activation of coagulation (plasma levels of prothrombin fragment F1 + 2 and thrombin-antithrombin III complexes). TNFR:Fc strongly inhibited endothelial cell activation (plasma levels of soluble E-selectin), modestly reduced **neutrophil** responses (neutrophilia and plasma concentrations of elastase-alpha-1-antitrypsin complexes and **lactoferrin**), but did not affect the release of secretory phospholipase A-2 or lipopolysaccharide-binding protein (P gt .05). Infusion of TNFR:Fc only (without LPS) in another 6 normal subjects did not induce any **inflammatory** response. These data indicate that TNF is involved in only some **inflammatory** responses to

intravenous LPS in **humans**.

L43 ANSWER 10 OF 19 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1996:288795 BIOSIS
DOCUMENT NUMBER: PREV199699011151
TITLE: Eosinophil and **neutrophil** activity in asthma in a one-year trial with inhaled budesonide: The impact of smoking.
AUTHOR(S): Pedersen, Bente; Dahl, Ronald; Karlstrom, Roberta; Peterson, Christer G. B.; Venge, Per [Reprint author]
CORPORATE SOURCE: Asthma Res. Centre, Dep. Clinical Chem., University Hosp., Uppsala S-751 85, Sweden
SOURCE: American Journal of Respiratory and Critical Care Medicine, (1996) Vol. 153, No. 5, pp. 1519-1529.
ISSN: 1073-449X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Jun 1996
Last Updated on STN: 25 Jun 1996

AB The object of this investigation was to study the long-term effects of antiasthma treatment on blood markers of **inflammation** and lung function in adult asthmatic subjects. For this purpose 85 allergic and nonallergic asthmatic subjects were randomized into three groups, which were given high-dose (1,600 mu-g/d) inhaled budesonide, low-dose (400 mu-g/d) inhaled budesonide, and **oral** theophylline (600 mg/d), respectively, and were followed for 11 mo with testing of lung function and blood sampling for the assay in serum of eosinophil cationic protein (ECP), eosinophil protein x/eosinophil derived neurotoxin (EPX/EDN) as eosinophil markers, and myeloperoxidase (MPO) and **lactoferrin** (LF) as **neutrophil** markers. Lung functions (FEV-1% predicted, and histamine PC-20) and the eosinophil markers ECP and EPX/EDN were improved and reduced, respectively, by budesonide in a dose-dependent and temporally parallel fashion. Theophylline did not alter lung functions but reduced ECP and EPX/EDN after prolonged treatment. The treatment efficacy of budesonide was attributed solely to an effect on nonsmoking asthmatic subjects, since neither lung functions nor eosinophil markers changed in smokers even with high-dose budesonide. MPO but not LF was reduced after several months of treatment in all three groups, but only in nonsmokers. We conclude that ECP and EPX/EDN may be used to monitor antiinflammatory treatment in asthmatic patients, and that smoking asthmatic subjects are resistant to inhaled corticosteroids.

L43 ANSWER 11 OF 19 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1994:253701 BIOSIS
DOCUMENT NUMBER: PREV199497266701
TITLE: Acute-phase proteins in gingival crevicular fluid during experimentally induced gingivitis.
AUTHOR(S): Adonogianaki, Evagelia [Reprint author]; Moughal, N. A.; Mooney, J.; Stirrups, D. R.; Kinane, D. F.
CORPORATE SOURCE: Unit Periodontol., Dep. Adult Dent. Care, Glasgow Dent. Hosp. Sch., 378 Sauchiehall St., Glasgow G2 3JZ, UK
SOURCE: Journal of Periodontal Research, (1994) Vol. 29, No. 3, pp. 196-202.
CODEN: JPDRAY. ISSN: 0022-3484.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Jun 1994
Last Updated on STN: 9 Jun 1994

AB The dynamics of four acute-phase proteins were investigated in gingival crevicular fluid (GCF) during the course of a 21 day experimental gingivitis study. These acute-phase proteins were the protease inhibitors alpha-2-macroglobulin (alpha-2-M) and alpha-1-antitrypsin (alpha-1-AT) and

the iron-binding proteins transferrin (TF) and **lactoferrin** (LF). 6 healthy volunteers ceased all **oral** hygiene procedures for 3 weeks. GCF was sampled at seven day intervals from two sites per subject by paper strips for 30 s during the experimental gingivitis period and for two additional weeks after the reinstitution of **oral** hygiene. The mainly serum derived alpha-2-M, alpha-1-AT and TF exhibited very similar dynamics which reflects their common origin in GCF. Their levels increased significantly from baseline and remained high for at least one week after the reinstitution of **oral** hygiene measures (repeated measures MANOVA: alpha-2-M: $p = 0.015$; alpha-1-AT: $p = 0.012$; TF: $p = 0.02$). This probably reflects increased vascular permeability in the gingivae and, to a lesser degree, local production by gingival **inflammatory** cells. In contrast to the serum derived acute-phase proteins, the **neutrophil** derived LF rose significantly from baseline (repeated measures MANOVA: $p = 0.001$) but dropped rapidly after the reinstitution of **oral** hygiene measures. This could be because dental plaque was removed and thus **neutrophil** chemotactic agents in the crevice were decreased.

L43 ANSWER 12 OF 19 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1993:258377 BIOSIS
DOCUMENT NUMBER: PREV199395137552
TITLE: Nasal secretions in response to acetylsalicylic acid.
AUTHOR(S): Kowalski, Marek L. [Reprint author]; Sliwinska-Kowalska, Mariola; Igarashi, Yasushi; White, Martha V.; Wojciechowska, Barbara; Brayton, Phyllis; Kaulbach, Helen; Rozniecki, Jerzy; Kaliner, Michael A.
CORPORATE SOURCE: Dep. Pulmonol. Allergol., Med. Acad., ul. Kopcinskiego 22, 90-153 Lodz, Poland
SOURCE: Journal of Allergy and Clinical Immunology, (1993) Vol. 91, No. 2, pp. 580-598.
CODEN: JACIBY. ISSN: 0091-6749.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 21 May 1993
Last Updated on STN: 13 Jul 1993

AB Background: Acetylsalicylic acid (ASA) induces rhinorrhea in a subset of patients with asthma or chronic rhinosinusitis or both and nasal polyps. The underlying mechanism of the reaction is obscure. Methods: To assess the nasal response to ASA challenge, four groups of patients were challenged **orally** with ASA: group A (10 ASA-sensitive patients); group B (nine patients with nasal polyps and histories of tolerance to ASA); group C (nine ASA-tolerant patients with chronic allergic rhinitis); and group D (eight healthy nonatopic subjects). Results: Nasal lavages obtained before and after ASA challenge were assayed for proteins (total protein, **lactoferrin**, lysozyme, **albumin**) and **inflammatory** mediators (histamine, prostaglandin D-2, and leukotriene C-4). ASA challenges induced severe rhinorrhea and congestion and significant increases in mean concentrations of all measured nasal proteins in group A. Histamine and prostaglandin D-2 rose, but not significantly. In the two control groups with chronic rhinitis, ASA induced increases in the concentration of proteins and histamine. Leukotriene C-4 concentrations were significantly elevated in nasal lavages after ASA challenge in groups A and C only. In group D no symptoms or changes in nasal proteins were observed after aspirin challenge. Conclusions: These observations suggest that production of lipoxygenase products of arachidonate may induce glandular secretions that may participate in the clinical changes associated with ASA sensitivity.

L43 ANSWER 13 OF 19 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1993:7842 BIOSIS
DOCUMENT NUMBER: PREV199395007842

Searched by: Mary Hale 571-272-2507 REM 1D86

TITLE: K562 cells produce an anti-**inflammatory** factor that inhibits **neutrophil** functions in vivo.
AUTHOR(S): Amar, M.; Amit, N.; Scoazec, J. Y.; Pasquier, C.; Babin-Chevaye, C.; Huu, T. Pham; Hakim, J. [Reprint author]
CORPORATE SOURCE: Lab. d'Hematol., CHU Xavier Bichat, 46 Rue Henri Huchard, 75877 Paris Cedex 18, France
SOURCE: Blood, (1992) Vol. 80, No. 6, pp. 1546-1552.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1992
Last Updated on STN: 13 Dec 1992

AB We have previously reported that K562, a chronic myelogenous leukemia cell line, releases a low molecular weight factor (6 to 8 Kd) that inhibits **human** polymorphonuclear **neutrophil** (PMN) adherence and adherence-related functions tested in vitro. We now report that this factor, which we have named K562 inhibitory factor (K562-IF), has potent anti-**inflammatory** activity in mice, associated with an inhibition of PMN functions. Its in vitro actions were less marked with mouse PMN than with **human** PMN. They included (1) an inhibition of both nonstimulated locomotion and locomotion induced by FMLP or serum; (2) an inhibition of the chemiluminescence induced by opsonized zymosan, but not that induced by phorbol myristate acetate or FMLP; (3) an inhibition of the degranulation stimulated by opsonized zymosan, as reflected by **lactoferrin** and lysozyme release; and (4) a decrease in arachidonic acid release and leukotriene B-4 production by A23187-stimulated PMN. The in vivo actions of K562-IF after **intraperitoneal injection** included (1) an inhibition of subcutaneous PMN accumulation at the site of **injection** of opsonized zymosan (PMN accumulated neither outside the vessels nor intravascularly, as shown by means of histochemistry); (2) an inhibition of **neutrophil** accumulation in the peritoneum of mice having received sodium caseinate or opsonized zymosan intraperitoneally; and (3) lysozyme concentration in **neutrophils** having reached the peritoneum after opsonized zymosan treatment equal to that in blood, suggesting diminished release. PMN influx and degranulation in the peritoneum were reduced by 50% after 3 hours of treatment with 1 mu-g of K562-IF (equivalent to the effect of 120 mu-g of prednisolone). Taken together, these results show that K562-IF is a potent anti-**inflammatory** agent that acts by inhibiting PMN functions.

L43 ANSWER 14 OF 19 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1992:391542 BIOSIS
DOCUMENT NUMBER: PREV199294063717; BA94:63717
TITLE: LONGITUDINAL STUDY OF PAROTID SALIVA IN HIV-1 INFECTION.
AUTHOR(S): MANDEL I D [Reprint author]; BARR C E; TURGEON L
CORPORATE SOURCE: COLUMBIA UNIVERSITY SCH, DENTAL ORAL SURGERY, 630 WEST 168TH ST, NEW YORK, NEW YORK 10032, USA
SOURCE: Journal of Oral Pathology and Medicine, (1992) Vol. 21, No. 5, pp. 209-213.
ISSN: 0904-2512.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 24 Aug 1992
Last Updated on STN: 25 Aug 1992

AB Parotid flow rate and chemistry of 78 HIV + gay/bisexual men and 27 HIV-gay/bisexual controls were compared on a longitudinal basis at 4-month intervals over a 1 yr period for changes indicative of **inflammatory** or autoimmune diseases of the salivary glands, or reduced protective capacity toward **oral** opportunistic infection. Parotid saliva was examined for concentrations of sodium, chloride,

phosphate, total protein, lysozyme, **lactoferrin**, secretory IgA, salivary peroxidase, histatin and **albumin**. Chloride, lysozyme and peroxidase were significantly higher in HIV+ at all 3 examinations and increased in concentration over time. Although mean values for stimulated flow rate were not significantly different in the two groups over the year, there was a significant increase in the number of HIV+ with reduced flow over time. In 6% of HIV+ there was a marked reduction in flow rate and Sjogren's syndrome-like elevations in parotid chemistry but no enlargement. At all examinations low flow rate was significantly related to **oral** candidiasis; T4 levels were inversely related to **oral** candidiasis, but not to concentration of salivary components or flow rate; nor was AZT use. As a group the HIV+ patients maintained normal flow rate and secreted normal or elevated concentrations of protective proteins. A subgroup, however, exhibited diminished flow over time and an increasing tendency to **oral** candidiasis and a diminution in output of histatins.

L43 ANSWER 15 OF 19 JICST-EPlus COPYRIGHT 2004 JST on STN
ACCESSION NUMBER: 920012359 JICST-EPlus
TITLE: **Oral** challenge with cow's milk in patients with IgA nephropathy. Estimation of serum antibodies to cow's milk protein.
AUTHOR: KOJIMA HIROOMI
CORPORATE SOURCE: Showa Univ., Fujigaoka Hospital
SOURCE: Nihon Jinzo Gakkaishi (Japanese Journal of Nephrology), (1991) vol. 33, no. 10, pp. 961-971. Journal Code: Z0142A (Fig. 6, Tbl. 4, Ref. 29)
ISSN: 0385-2385
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New
AB The author investigated the serum levels of antibodies against casein, B- **lactoglobulin** and lactalbumin before and after challenging with cow's milk in 35 patients with IgA enphropathy, 18 with primary glomerulonephritis except for IgA nephropathy (GN control) and 11 healthy volunteers (H control). Blood samples were obtained at fasting, and at 30,60,120 and 180min after **oral** challenging with 400ml of cow's milk. IgA and IgG anti-cow's milk proteins antibodies were analyzed by ELISA. The same challenge was tested after administration of the antiallergic agent, sodium cromoglycate(SCG), in 11 patients with IgA nephropathy and 4H controls. Serum levels of IgA anti-casein, -B- **lactoglobulin** and lactalbumin antibodies in patients with IgA nephropathy were significantly higher than in control groups before challenging. However, those of IgG antibodies were not. The percent change of antibody titer after challenging with cow's milk did not elevate in any group, except for the level of IgA anti-B- **lactoglobulin** antibody at 60min in IgA nephropathy. Cases in which challenging produced marked elevation above the M+2SD of the levels found in H control were expressed as "positive". The number of "positive" cases was 16 (45.7%) with IgA nephropathy, but none with GN control. There was no significant correlations between "positive" and "negative" cases with IgA nephropathy in clinical manifestations. In 3 out of 4 "positive" patients with IgA nephropathy, the levels of IgA antibody were suppressed after administration of SCG. (abridged author abst.)

L43 ANSWER 16 OF 19 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1991:250821 BIOSIS
DOCUMENT NUMBER: PREV199191131376; BA91:131376
TITLE: **INFLAMMATORY** MARKERS IN CYSTIC FIBROSIS.
AUTHOR(S): RAYNER R J [Reprint author]; WISEMAN M S; CORDON S M; NORMAN D; HILLER E J; SHALE D J

Searched by: Mary Hale 571-272-2507 REM 1D86

CORPORATE SOURCE: RESPIRATORY MEDICINE UNIT, UNIVERSITY NOTTINGHAM, CITY HOSPITAL, HUCKNALL ROAD, NOTTINGHAM NG5 1PB, UK
SOURCE: Respiratory Medicine, (1991) Vol. 85, No. 2, pp. 139-146. ISSN: 0954-6111.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 25 May 1991
Last Updated on STN: 25 May 1991

AB Plasma **neutrophil** elastase-α1 antiproteinase complex, **lactoferrin** and C-reactive protein (CRP) were determined over a 15-month period in 26 patients with cystic fibrosis, of whom 21 were chronically infected with Pseudomonas aeruginosa. Median concentrations of both **neutrophil** products and CRP were greater in patients who were clinically stable than in healthy subjects without cystic fibrosis. CRP concentrations increased further at the onset of symptomatic exacerbations. Thirty-five courses of intravenous antibiotics and 22 courses of **oral** ciprofloxacin were reviewed and revealed similar improvements in clinical scores and lung function tests for both forms of treatment. Intravenous antibiotics reduced the plasma concentrations of both **neutrophil** products and CRP, while **oral** ciprofloxacin only significantly reduced the concentration of **neutrophil** elastase-α1 antiproteinase complex. Plasma concentrations of **inflammatory** markers were significantly greater in exacerbations associated with fever and leukocytosis. Statistical modelling demonstrated negative within-patient relationships between lung function and both CRP and **lactoferrin**, and positive relationships between the three **inflammatory** markers. **Neutrophil** granule products and CR reflect the pulmonary **inflammatory** state in cystic fibrosis and may be of value in monitoring treatment.

L43 ANSWER 17 OF 19 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1991:4955 BIOSIS
DOCUMENT NUMBER: PREV199191004955; BA91:4955
TITLE: THE **NEUTROPHIL**-ACTIVATING PROTEINS INTERLEUKIN 8 AND BETA THROMBOGLOBULIN IN-VITRO AND IN-VIVO COMPARISON OF AMINO-TERMINALLY PROCESSED FORMS.
AUTHOR(S): VAN DAMME J [Reprint author]; RAMPART M; CONINGS R; DECOCK B; VAN OSSELAER N; WILLEMS J; BILLIAU A
CORPORATE SOURCE: REGA INST MED RES, UNIV LEUVEN, MINDERBRODERSTRAAT 10, B-3000 LEUVEN, BELG
SOURCE: European Journal of Immunology, (1990) Vol. 20, No. 9, pp. 2113-2118.
CODEN: EJIMAF. ISSN: 0014-2980.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 8 Dec 1990
Last Updated on STN: 8 Dec 1990

AB Isolation of the **human neutrophil** activating protein (NAP) interleukin 8 (IL8) from leukocytes has revealed that it is structurally related to β-thromboglobulin (βTG) from platelets. Both these proteins occur as natural mixtures of multiple forms, differing from each other by unequal truncation of the NH2 terminus. In this study we have compared IL8 and βTG forms for in vitro and in vitro **neutrophil** activation. In contrast to IL8, none of the βTG forms were found to exert granulocyte chemotactic activity in vitro, as measured in the agarose assay. However, fractions rich in the most extensively processed forms of βTG (e.g. NAP-2) as well as pure NAP-2 did induce **lactoferrin** release from granulocytes, whereas fractions containing only the longer forms (e.g. connective

tissue-activating peptide III) were inactive. In order to observe this in vitro effect, about 10-fold less IL8 (10 nM) than NAP-2 was required. In the presence of a vasodilatator substance low doses (2-20 pmol) of IL8 and the shorter forms of βTG caused granulocyte accumulation and plasma leakage in rabbit skin whereas the longer forms of βTG again failed to do so. Finally granulocytosis induction following i.v. **injection** was found to occur with NAP-2. At the maximal dose tested (250 pmol), this in vivo effect of NAP-2 was less pronounced than that of IL8. In the case of IL8, NH2-terminal processing did not seem to affect granulocyte stimulatory activity. It should be noted, however, that the extent of processing of IL8 is less than that occurring with βTG. It can be concluded that the platelet factor βTG, structurally related to the monokine IL8, can also play a role in **neutrophil** activation during **inflammatory** reactions.

L43 ANSWER 18 OF 19 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1989:98175 BIOSIS
DOCUMENT NUMBER: PREV198987052311; BA87:52311
TITLE: **ORAL** N ACETYLCYSTEINE REDUCES SELECTED HUMORAL MARKERS OF **INFLAMMATORY** CELL ACTIVITY IN BAL FLUID FROM HEALTHY SMOKERS CORRELATION TO EFFECTS OF CELLULAR VARIABLES.
AUTHOR(S): EKLUND A [Reprint author]; ERIKSSON O; HAKANSSON L; LARSSON K; OHLSSON K; VENGE P; BERGSTRAND H; BJORNSON A; BRATTSAND R; ET AL
CORPORATE SOURCE: RES AND DEV DEP, PHARMACOL LAB, AB DRACO, BOX 34, S-221 00 LUND, SWEDEN
SOURCE: European Respiratory Journal, (1988) Vol. 1, No. 9, pp. 832-838.
CODEN: ERJOEI. ISSN: 0903-1936.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 6 Feb 1989
Last Updated on STN: 6 Feb 1989

AB Bronchoalveolar lavage (BAL) was performed on eleven healthy smokers before and after eight weeks of **oral** treatment with N-acetylcysteine (NAC) 200 mg t.i.d. The concentrations of selected eosinophil and **neutrophil** granule constituents and of selected proteases and protease inhibitors, **albumin** and endotoxin were determined in the recovered BAL fluid and in plasma or serum samples. In addition, in vitro chemotactic activities for **neutrophils** and eosinophils were assessed in the BAL fluid. Significantly reductions in BAL fluid content of **lactoferrin** (LF), eosinophil cationic protein (ECP), antichymotrypsin (ACT) and chemotactic activity for **neutrophils** were recorded after NAC treatment. The levels of other examined markers tended to be reduced or were not affected. In serum/plasma, the concentrations of myeloperoxidase (MPO) and elastase were reduced after NAC treatment whereas concentrations of other constituents examined were unaltered. These data, together with previously reported findings, suggest that **oral** NAC may influence the activity of "**inflammatory**" cells in the bronchoalveolar space of smokers.

L43 ANSWER 19 OF 19 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1987:46697 BIOSIS
DOCUMENT NUMBER: PREV198783026043; BA83:26043
TITLE: CHANGES IN THE PROTEIN COMPOSITION OF WHOLE SALIVA DURING RADIOTHERAPY IN PATIENTS WITH **ORAL** OR PHARYNGEAL CANCER.
AUTHOR(S): MAKKONEN T A [Reprint author]; TENOVUO J; VILJA P; HEIMDAHL A

Searched by: Mary Hale 571-272-2507 REM 1D86

CORPORATE SOURCE: INST DENTISTRY, UNIV TURKU, LEMMINKAISENKATU 2, SF-20520 TURKU, FINLAND
SOURCE: Oral Surgery Oral Medicine Oral Pathology, (1986) Vol. 62, No. 3, pp. 270-275.
CODEN: OSOMAE. ISSN: 0030-4220.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 7 Jan 1987
Last Updated on STN: 7 Jan 1987

AB We analyzed the radiation-induced changes in the flow rate and protein composition of stimulated whole saliva in eleven patients treated for malignant conditions on the head and neck. In all patients the radiation field covered all major salivary glands and a large area of the **oral** mucosa. Paraffin-stimulated whole saliva samples were collected once 2 to 21 days before therapy and then after 20, 40, and 60 gray (Gy) cumulative dose of irradiation. Five patients also provided samples 6 months after the therapy. Hyposalivation or xerostomia occurred in all patients, although the pretreatment secretion rates were already relatively low. Salivary amylase activities decreased with increasing dose of radiation, especially when expressed as the amount of enzyme secreted per minute. Unusually high salivary concentrations of **albumin**, **lactoferrin**, lysozyme, salivary peroxidase, myeloperoxidase, and total protein were observed during the therapy, but most values slowly returned to pretreatment levels after cessation of radiation. It is concluded that the observed qualitative changes in whole saliva components are net effects caused by the cancer itself, radiation therapy given, systemic diseases, or medications, as well as mucosal **inflammations**.

L58 ANSWER 1 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2004:131103 BIOSIS
DOCUMENT NUMBER: PREV200400132642
TITLE: Fas ligand mediates immune privilege and not **inflammation** in human colon cancer, irrespective of TGF-beta expression.
AUTHOR(S): Houston, A.; Bennett, M. W.; O'Sullivan, G. C.; Shanahan, F.; O'Connell, J. [Reprint Author]
CORPORATE SOURCE: Department of Medicine, National University of Ireland, University Hospital, Clinical Sciences Building, Cork, Ireland
J.OConnell@ucc.ie
SOURCE: British Journal of Cancer, (6 October 2003) Vol. 89, No. 7, pp. 1345-1351. print.
ISSN: 0007-0920 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Mar 2004
Last Updated on STN: 10 Mar 2004

AB Many cancers express Fas ligand (FasL/CD95L) in vivo, and can kill lymphoid cells by Fas-mediated apoptosis in vitro. However, overexpression of recombinant FasL in murine tumour allografts revealed a potential antitumour effect of FasL, via recruitment of **neutrophils**. Transforming growth factor-beta1 (TGF-beta1) could inhibit these **neutrophil**-stimulatory effects of FasL. In the present study, we sought to determine directly whether FasL contributes to immune privilege or tumour rejection in human colon cancers in vivo, and whether TGF-beta1 regulates FasL function. Serial tumour sections were immunostained for FasL and TGF-beta1. **Neutrophils** and tumour

infiltrating lymphocytes (TILs) were detected by immunohistochemistry for **lactoferrin** and CD45, respectively. Apoptotic TIL were identified by dual staining for TUNEL/CD45. FasL expression by nests of tumour cells was associated with a mean four-fold depletion of TILs (range 1.8-33-fold, n=16, P<0.001), together with a two-fold increase in TIL apoptosis (range 1.6-2.5-fold, n=14, P<0.001), relative to FasL-negative nests within the same tumours. The overall level of **neutrophils** present in all tumours examined was low (mean 0.3%, n=16), with FasL expression by tumour nests associated with a mean two-fold decrease in **neutrophils**, irrespective of TGF-beta1 expression. Together, our result suggest that tumour-expressed FasL is inhibitory rather than stimulatory towards antitumour immune responses.

L58 ANSWER 2 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:116121 BIOSIS
DOCUMENT NUMBER: PREV200300116121
TITLE: Anti-**inflammatory** activities of human **lactoferrin** in acute dextran sulphate-induced colitis in mice.
AUTHOR(S): Haversen, L. A. [Reprint Author]; Baltzer, L.; Dolphin, G.; Hanson, L. A.; Mattsby-Baltzer, I.
CORPORATE SOURCE: Department of Clinical Bacteriology, University of Goteborg, Guldhedsgatan 10, S-41346, Goteborg, Sweden liliana.ceafalau@microbio.gu.se
SOURCE: Scandinavian Journal of Immunology, (January 2003) Vol. 57, No. 1, pp. 2-10. print.
ISSN: 0300-9475 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Feb 2003
Last Updated on STN: 26 Feb 2003

AB In this study, we investigated the anti-**inflammatory** effects of orally administered human **lactoferrin** (hLF) and two peptides, based on the bactericidal region of hLF (HLD1 and HLD2), on the course of experimental colitis. Acute colitis was induced in C57Bl/6 mice by giving 5% dextran sulphate (DX) in the drinking water. The mice were killed after 2 or 7 days of DX exposure. The animals were given hLF or the peptides orally twice a day (2 mg/dose/mouse) during the DX exposure. In the control animals, the hLF or the peptides were replaced by bovine serum **albumin** or water. The appearance of occult blood in the faeces and macroscopic rectal bleeding were significantly delayed and partly reduced in the hLF-treated animals compared with the control animals. The shortening of the colon, a pathological effect of DX exposure, was significantly less pronounced in the hLF-treated group compared with the control group. Also, the interleukin-1beta (IL-1beta) levels in the blood were significantly diminished in this group after 2 days of DX exposure. A significantly lower crypt score was observed in the distal part of the colon in the hLF-treated group compared with the control group. Also, significantly reduced numbers of CD4 cells, F4/80-positive macrophages and tumour necrosis factor-alpha-producing cells were detected by immunohistochemistry in the distal colon of the hLF-treated animals compared with the control animals after 7 days of DX exposure. A reduction was also observed concerning the IL-10-producing cells in the middle colonic submucosa. The HLD1 and HLD2 treatment, which was carried out for 2 days, only gave results almost identical to those of hLF, concerning clinical parameters after the 2 days of DX exposure. An even stronger effect was observed for HLD2, regarding decreased occult blood in the faeces and colon length. Our results show that perorally given hLF mediates anti-**inflammatory** effects on the DX-induced acute colitis, and further suggest that the bactericidal region of the hLF molecule may be involved in these activities.

L58 ANSWER 3 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:517168 BIOSIS
DOCUMENT NUMBER: PREV200300519790
TITLE: The **inflammatory** response of intestinal epithelial cells to enteroaggregative Escherichia coli.
AUTHOR(S): Harrington, S. M. [Reprint Author]; Abe, C. M.; Nataro, J. P. [Reprint Author]
CORPORATE SOURCE: University of Maryland, Baltimore, Baltimore, MD, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2003) Vol. 103, pp. B-036. http://www.asmusa.org/mtgsrc/generalmeeting.htm. cd-rom. Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003. American Society for Microbiology. ISSN: 1060-2011 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Nov 2003
Last Updated on STN: 5 Nov 2003

AB Enteroaggregative E. coli (EAEC) causes persistent, watery diarrhea that may be mildly **inflammatory**. Specifically, **lactoferrin**, IL-8 and IL-1beta have been detected in feces from cases of EAEC diarrhea. To determine if other **inflammatory** mediators might be induced we infected T84 cells with EAEC prototype strain 042 from an overnight L broth culture and hybridized a human cytokine macroarray with cellular cDNA. In addition to IL-8, several genes characteristic of an acute bacterial infection were induced greater than 3-fold. These included IL-6, **TNF-alpha**, the GRO chemokines, ICAM-1, GM-CSF, iNOS, fractalkine, IL-1alpha, integrin-beta2, 4-1BB, and MCP-3. The induction of several **inflammatory** markers including IL-8, **TNF-alpha**, IL-6 and IL-1beta was further confirmed with RT-PCR. The flagellin of EAEC has been shown to induce IL-8 from intestinal epithelial cells (IECs) in culture, and thus may contribute to the observed clinical response. Recently, Jiang et al. showed that fecal IL-8 and IL-1beta were associated with infection with EAEC strains having one or more plasmid-borne virulence factors. Using conditions to enhance expression of plasmid-borne genes, we assessed the contribution of the plasmid-encoded fimbrial subunit (aafA) and the dispersin (aap) genes with a real-time PCR assay for IL-8 mRNA induction by infected HT-29 cells. As expected, a flagellar mutant (042fliC) induced less IL-8 (3 to 6 fold) compared to 042 infected cells. However, both 042aafA and 042aap caused a subtle, but consistent increase (approximately 2 fold) in IL-8 above levels induced by 042. These data suggest that AAF/II and dispersin are not proinflammatory, but may instead modulate the **inflammatory** response either directly, or by modifying the expression of flagellin or an as yet uncharacterized factor.

L58 ANSWER 4 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:50516 BIOSIS
DOCUMENT NUMBER: PREV200300050516
TITLE: Oral administration of **lactoferrin** reduces colitis in rats via modulation of the immune system and correction of cytokine imbalance.
AUTHOR(S): Togawa, Jun-ichi [Reprint Author]; Nagase, Hajime; Tanaka, Katsuaki; Inamori, Masahiko; Nakajima, Atsushi; Ueno, Norio; Saito, Toshifumi; Sekihara, Hisahiko
CORPORATE SOURCE: Third Department of Internal Medicine, Yokohama City University School of Medicine, 3-9 Fuku-ura, Kanazawa-ku, Yokohama, 236-0004, Japan
j_togawa@med.yokohama-cu.ac.jp
SOURCE: Journal of Gastroenterology and Hepatology, (December 2002)

Searched by: Mary Hale 571-272-2507 REM 1D86

Vol. 17, No. 12, pp. 1291-1298. print.
CODEN: JGHEEO. ISSN: 0815-9319.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Jan 2003
Last Updated on STN: 15 Jan 2003

AB Background and Aims: The natural immunomodulator, **lactoferrin**, is widespread among various biological fluids and is known to exert an anti-**inflammatory** effect. However, there has been only one study that examined the mode of action of **lactoferrin** in reducing intestinal damage. We investigated the therapeutic role of **lactoferrin** and its effect on the levels of pro-**inflammatory** and anti-**inflammatory** cytokines, by using a rat model of dextran sulfate sodium (DSS) induced-colitis. Methods: Male Sprague-Dawley rats were given distilled drinking water containing 2.5% (wt/vol) synthetic DSS ad libitum. Bovine **lactoferrin** was given once daily through gavage, starting 3 days before beginning the DSS administration, until death. The whole colon was removed to be examined macroscopically and histologically. Myeloperoxidase activity, and pro-**inflammatory** and anti-**inflammatory** cytokines in the colonic tissue were also measured. Results: Dextran sulfate sodium-induced colitis was attenuated by oral administration of **lactoferrin** in a dose-dependent manner, as reflected by improvement in clinical disease activity index, white blood cell count and hemoglobin concentration, macroscopic and histological scores, and myeloperoxidase activity. Reduced **inflammation** in response to **lactoferrin** was correlated with the significant induction of the anti-**inflammatory** cytokines, interleukin-4 and interleukin-10, and with significant reductions in the pro-**inflammatory** cytokines, **tumor necrosis factor alpha**, interleukin-1beta, and interleukin-6. Conclusions: We concluded that oral administration of **lactoferrin** exerts a protective effect against the development of colitis in rats via modulation of the immune system and correction of cytokine imbalance. **Lactoferrin** has potential as a new therapeutic agent for **inflammatory** bowel disease.

L58 ANSWER 5 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:447817 BIOSIS
DOCUMENT NUMBER: PREV200200447817
TITLE: **Lactoferrin** reduces colitis in rats via modulation of the immune system and correction of cytokine imbalance.
AUTHOR(S): Togawa, Jun-ichi [Reprint author]; Nagase, Hajime; Tanaka, Katsuaki; Inamori, Masahiko; Umezawa, Tadashi; Nakajima, Atsushi; Naito, Makoto; Sato, Shinobu; Saito, Toshifumi; Sekihara, Hisahiko
CORPORATE SOURCE: Third Dept. of Internal Medicine, Yokohama City Univ. School of Medicine, 3-9 Fuku-ura, Kanazawa-ku, Yokohama, 236-0004, Japan
j_togawa@med.yokohama-cu.ac.jp
SOURCE: American Journal of Physiology, (July, 2002) Vol. 283, No. 1 Part 1, pp. G187-G195. print.
CODEN: AJPHAP. ISSN: 0002-9513.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Aug 2002
Last Updated on STN: 21 Aug 2002

AB Natural immunomodulator **lactoferrin** is known to exert an anti-**inflammatory** effect. However, there have been no studies that examine the mode of action of **lactoferrin** in reducing intestinal damage. We investigated the effect of **lactoferrin** on a

trinitrobenzenesulfonic acid (TNBS)-induced colitis model in rats. Bovine **lactoferrin** was given once daily through gavage, starting 3 days before (preventive mode) or just after TNBS administration (treatment mode) until death. The distal colon was removed to be examined. Colitis was attenuated by **lactoferrin** via both modes in a dose-dependent manner, as reflected by improvement in macroscopic and histological scores and myeloperoxidase activity. **Lactoferrin** caused significant induction of the anti-**inflammatory** cytokines interleukin (IL)-4 and IL-10, significant reductions in the proinflammatory cytokines **tumor necrosis factor-alpha** and IL-1beta, and downregulation of the nuclear factor-kappaB pathway. We concluded that **lactoferrin** exerts a protective effect against colitis in rats via modulation of the immune system and correction of cytokine imbalance. **Lactoferrin** has potential as a new therapeutic agent for **inflammatory** bowel disease.

L58 ANSWER 6 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:234498 HCAPLUS
TITLE: Molecular mechanisms of inhibition of **neutrophil** recruitment by **lactoferrin**
AUTHOR(S): Baveye, S.; Elass, E.; Blanquart, C.; Masson, M.; Mazurier, J.; Legrand, D.
CORPORATE SOURCE: Unite Mixte de Recherche du CNRS no 8576, Universite des Sciences et Technologies de Lille, Villeneuve d'Ascq, 59655, Fr.
SOURCE: Biochemistry and Cell Biology (2002), 80(1), 164
CODEN: BCBIEQ; ISSN: 0829-8211
PUBLISHER: National Research Council of Canada
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lipopolysaccharides (LPS) are elicitors of the immune system and are potent stimulators of **inflammation** by acting on both leukocytes and endothelial cells. LPS activate polynuclear **neutrophils**, which in turn, produce abundant reactive oxygen species important for the killing of **ingested** microorganisms and for cell-mediated cytotoxicity. Such a defense mechanism is triggered by the plasma LPS-binding protein (LBP), which catalyzes the transfer of LPS to CD14, a glycosylphosphatidyl inositol-anchored mol. present on monocyte macrophages, and to a lesser extent on **neutrophils**. However, at high LPS doses, other pathways participate to the activation of **neutrophils**, that leads to the overprodn. of oxygen free radicals and subsequent damaging of host tissues. The activation of leukocytes by LPS, resulting in the oxidative burst, contributes to the pathogenesis of septic shock. L-selectin, a cell-surface integral membrane glycoprotein involved in leukocytes trafficking, thrombosis, and **inflammation** , was shown to mediate both LPS binding and signal transduction on **neutrophils**. The binding of LPS to L-selectin induces the production of oxygen free radicals. The interaction of LPS with L-selectin is serum- and calcium-independent and induces the production of superoxide and hydrogen peroxide. Simultaneously, LPS induces the expression of adhesion mols. such as endothelial-leukocyte adhesion mol.-1 (E-selectin) and intercellular adhesion mol.-1 (ICAM-1) by endothelial cells and initiates the recruitment of circulating leukocytes at **inflammatory** tissue sites. Endotoxin stimulation of endothelial cells is mediated by soluble CD14 (sCD14), a specific LPS receptor. Human **lactoferrin**, an iron-binding glycoprotein released from **neutrophil** granules during infection, protects animals against septic shock. We demonstrate that the anti-**inflammatory** effects of **Lactoferrin** are due to (i) its ability to chelate the LPS and therefore to prevent the binding of LPS to L-selectinand forbidding the activation of **neutrophils**; and (ii) its ability to interact with soluble CD14 and the LPS-sCD14 complex thus modifying the activation of endothelial cells.

Searched by: Mary Hale 571-272-2507 REM 1D86

L58 ANSWER 7 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:234486 HCAPLUS
TITLE: **Lactoferrin**: bacterial opsonin for macrophages?
AUTHOR(S): Otsuki, K.; Lonnerdal, B.; Sherman, M. P.
CORPORATE SOURCE: Department of Obstetrics and Gynecology, School of Medicine, Showa University, Tokyo, Japan
SOURCE: Biochemistry and Cell Biology (2002), 80(1), 158
CODEN: BCBIEQ; ISSN: 0829-8211
PUBLISHER: National Research Council of Canada
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Because recombinant human **lactoferrin** (rh-LF) reportedly binds to endotoxin (LPS) and receptors on macrophages (M.vphi.), we asked if rh-LF could promote the **ingestion** of Escherichia coli by M.vphi.. We first tested whether rh-LF alone kills E. coli and stimulates M.vphi. to produce **TNF-α** and nitric oxide (NO). When proof existed that rh-LF bound to E. coli and M.vphi., we determined whether rh-LF acted as an opsonin for E. coli. Rh-LF was expressed in Aspergillus and purified after secretion. An assay using CO2-buffered medium studied whether rh-LF restricted E. coli growth. Rat M.vphi. were stimulated with rh-LF, and an ELISA and the Griess reaction measured **TNF-α** and nitrite in the supernatants, resp. Fluorescent E. coli were opsonized with NaCl, serum, LF, or LF + serum and incubated with M.vphi. at 50:1 ratio for 1 h at 37°C. **Ingestion** was measured with an extracellular dye quenching method that allows detection of bacteria **ingested** by M.vphi.. Using smooth and rough strains of E. coli, rh-LF was not an opsonin (5-19% **ingestion**). The rate of phagocytosis for NaCl = 6-21%, serum = 70-79%, and serum + LF = 68-81%. The phagocytic index (Number E. coli/ **ingesting** M.vphi.) was similar in the NaCl and rh-LF groups (M.vphi. E. coli/M.vphi.), while serum or serum + LF had 5-6 E. coli/M.vphi.. Human milk and bovine LF also were not opsonins. M.vphi. pre-treated with rh-LF and then stimulated with serum-opsonized E. coli increased their production of **TNF-α** and N (P < 0.01). In conclusion, rh-LF is not an opsonin for E. coli; rh-LF also did not block, but rather enhanced, the production of **TNF-.alpha** . and NO when opsonized E. coli were exposed to M.vphi. pre-treated with rh-LF. These findings question whether LF is a LPS-binding protein that reduces **inflammation** as previous studies suggest.

L58 ANSWER 8 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:342424 BIOSIS
DOCUMENT NUMBER: PREV200300342424
TITLE: Neurally mediated inhibition of gastric fundus motility following lipopolysaccharide-induced acute **inflammation.**
AUTHOR(S): Ceregrzyn, Michal [Reprint Author]; Kamata, Tadashi; Kuwahara, Atsukazu
CORPORATE SOURCE: Laboratory of Physiology, Institute for Environmental Sciences, University of Shizuoka, 52-1 Yada, Shizuoka, Shizuoka, 422-8526, Japan
gp1163@spost.u-shizuoka-ken.ac.jp
SOURCE: Biomedical Research (Tokyo), (June 2002) Vol. 23, No. 3, pp. 135-144. print.
CODEN: BRESD5. ISSN: 0388-6107.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003
AB The mechanism of endotoxemia-induced alterations in gastrointestinal

Searched by: Mary Hale 571-272-2507 REM 1D86

motility still remains unclear. The aim of the present study was to investigate the effect of bacterial lipopolysaccharide (LPS) on contractility of gastric fundus. Endotoxemia was induced by single injection of LPS (10 mg/kg) in mice. In vitro exposure to LPS was performed using rat gastric fundus. In vivo gastric emptying was measured in mice using the phenol red method. LPS induced significant reduction of electrically induced contractions of mouse gastric fundus. The effect of LPS was diminished by **tumor necrosis factor alpha** (**TNF-alpha**) production inhibitor, recombinant human **lactoferrin**. LPS inhibited responses to prostaglandin F2alpha (PGF2alpha) and 5-hydroxytryptamine (5-HT) but not to acetylcholine (ACh). Similar effects were observed after incubation of tissue with LPS. 5-HT- and KCl-induced contractions were smaller in tissues incubated with LPS for 8 h while response to ACh was not significantly changed. Gastric emptying was inhibited during endotoxemia. However at the time when maximal decrease in gastric fundus contractility was observed (8 h) gastric emptying was with control value. In conclusion, the effect of LPS on gastric motoric function is due to central and local actions of endotoxin and is mediated by **TNF-alpha** production.

L58 ANSWER 9 OF 33 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001435436 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11302825
TITLE: Thalidomide inhibits granulocyte responses in healthy humans after ex vivo stimulation with bacterial antigens.
AUTHOR: Juffermans N P; Verbon A; Schultz M J; Hack C E; van Deventer S J; Speelman P; van der Poll T
CORPORATE SOURCE: Laboratory of Experimental Internal Medicine, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands.
SOURCE: Antimicrobial agents and chemotherapy, (2001 May) 45 (5) 1547-9.
Journal code: 0315061. ISSN: 0066-4804.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010806
Last Updated on STN: 20010806
Entered Medline: 20010802

AB **Ingestion** of thalidomide was associated with a reduction in the upregulation of the granulocyte activation marker CD11b and a reduced capacity to release elastase and **lactoferrin** after stimulation with lipopolysaccharide or lipoteichoic acid. A single oral dose of thalidomide attenuates **neutrophil** activation upon ex vivo stimulation with bacterial antigens.

L58 ANSWER 10 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:235220 BIOSIS
DOCUMENT NUMBER: PREV200100235220
TITLE: Fecal calprotectin as an index of intestinal **inflammation**.
AUTHOR(S): Tibble, J. A.; Bjarnason, I. [Reprint author]
CORPORATE SOURCE: Department of Medicine, Guy's, King's, St. Thomas's Medical School, Bessemer Road, London, SE5 9PJ, UK
SOURCE: Drugs of Today, (February, 2001) Vol. 37, No. 2, pp. 85-96. print.
CODEN: MDACAP. ISSN: 0025-7656.
DOCUMENT TYPE: Article
LANGUAGE: English

Searched by: Mary Hale 571-272-2507 REM 1D86

ENTRY DATE: Entered STN: 16 May 2001
Last Updated on STN: 18 Feb 2002

AB The assessment of **inflammatory** activity in intestinal disease in man can be done using a variety of different techniques, from measurement of conventional noninvasive acute-phase **inflammatory** markers in plasma (C-reactive protein and the erythrocyte sedimentation rate) to the direct assessment of disease activity by intestinal biopsy. However, most of these techniques have significant limitations when it comes to assessing functional components of the disease that relate to activity and prognosis. Here we briefly review the value of a novel emerging intestinal function test, fecal calprotectin. Single stool assay of **neutrophil**-specific proteins (calprotectin, **lactoferrin**) give the same quantitative data on intestinal **inflam** mation as the 4-day fecal excretion of indium-111-labeled white cells. Elevated levels of fecal calprotectin have been demonstrated in patients with NSAID-induced enteropathy and have been used in the diagnosis of colorectal cancer. Fecal calprotectin is increased in over 95% of patients with **inflammatory** bowel disease (IBD) and correlates with clinical disease activity. It reliably differentiates between patients with IBD and irritable bowel syndrome (IBS). More importantly, at a given fecal calprotectin concentration in patients with quiescent IBD, the test has a specificity and sensitivity in excess of 85% in predicting clinical relapse of disease. This suggests that relapse of IBD is closely related to the degree of intestinal **inflammation** and suggests that targeted treatment at an asymptomatic stage of the disease may be indicated.

L58 ANSWER 11 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:268957 BIOSIS
DOCUMENT NUMBER: PREV200000268957
TITLE: Fecal **lactoferrin** as an indicator of disease activity in **Inflammatory** Bowel Disease (IBD).
AUTHOR(S): Boone, J. [Reprint author]; Lyerly, D.; Gelbmann, C.; Drexler, U.; Bregenzer, N.; Scholmerich, J.; Andus, T.
CORPORATE SOURCE: TechLab, Inc, Blacksburg, VA, USA
SOURCE: Gastroenterology, (April, 2000) Vol. 118, No. 4 Suppl. 2 Part 2, pp. AGA A1118. print.
Meeting Info.: 101st Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week. San Diego, California, USA. May 21-24, 2000. American Gastroenterological Association.
CODEN: GASTAB. ISSN: 0016-5085.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jun 2000
Last Updated on STN: 5 Jan 2002

L58 ANSWER 12 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:325399 BIOSIS
DOCUMENT NUMBER: PREV199900325399
TITLE: Investigation of **neutrophils** in the gut by analyses of whole-gut lavage fluid and feces in patients with **inflammatory** bowel disease.
AUTHOR(S): Saitoh, Osamu [Reprint author]; Kojima, Keishi [Reprint author]; Tanaka, Seigou [Reprint author]; Teranishi, Tsutomu [Reprint author]; Sugi, Kazunori [Reprint author]; Nakagawa, Ken [Reprint author]; Matsuse, Ryoichi; Tabata, Kazue; Uchida, Kazuo; Matsumoto, Hisashi; Hirata, Ichiro; Katsu, Ken-ichi
CORPORATE SOURCE: Osaka Med Coll, Takatsuki, Japan
SOURCE: Gastroenterology, (April, 1999) Vol. 116, No. 4 PART 2, pp.

Searched by: Mary Hale 571-272-2507 REM 1D86

A809. print.
Meeting Info.: Digestive Disease Week and the 100th Annual Meeting of the American Gastroenterological Association. Orlando, Florida, USA. May 16-19, 1999. American Gastroenterological Association.
CODEN: GASTAB. ISSN: 0016-5085.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Aug 1999
Last Updated on STN: 24 Aug 1999

L58 ANSWER 13 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:162884 BIOSIS
DOCUMENT NUMBER: PREV199800162884
TITLE: **Lactoferrin** impedes epithelial cell adhesion in vitro.
AUTHOR(S): Pollanen, Marja T. [Reprint author]; Hakkinen, L.; Overman, D. O.; Salonen, J. I.
CORPORATE SOURCE: Inst. Dent., Univ. Turku, FIN-20520 Turku, Finland
SOURCE: Journal of Periodontal Research, (Jan., 1998) Vol. 33, No. 1, pp. 8-16. print.
CODEN: JPDRAY. ISSN: 0022-3484.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Apr 1998
Last Updated on STN: 6 Apr 1998

AB In the process of host defence against microbial challenge, **neutrophils** release granule contents with the potential side effect of damaging structural tissues. In the junctional epithelium such damage may contribute to the degeneration and renewal of the epithelial cells attached directly to the tooth (DAT cells), and subsequently to periodontal pocket formation. This study reports on **lactoferrin**, one of the substances released by **neutrophils**, and its effects on epithelial cell adhesion, growth, DNA synthesis and spreading of cell colonies at concentrations recorded in the crevicular fluid. We show that, in opposition to what has been reported on bacterial cells, **lactoferrin** has no effect on the DNA synthesis of attached epithelial cells in model systems attempting to simulate the DAT cells in vivo. However both iron-saturated and unsaturated **lactoferrin** hampered cell adhesion, growth and spreading of cell colonies in a dose-dependent manner. These findings suggest that **lactoferrin** does not affect epithelial cell proliferation but it may have a role in delaying the repair of the DAT cell population during **inflammation** by interfering with cell adhesion.

L58 ANSWER 14 OF 33 MEDLINE on STN
ACCESSION NUMBER: 1998452036 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9779014
TITLE: The influence of radiographic contrast media on some granulocyte functions.
AUTHOR: Rasmussen F
SOURCE: Acta radiologica. Supplementum, (1998) 419 7-35. Ref: 294
Journal code: 0370370. ISSN: 0365-5954.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106

Searched by: Mary Hale 571-272-2507 REM 1D86

Last Updated on STN: 19990106
Entered Medline: 19981109

AB Radiographic CM are used to change the X-ray absorption of tissue. They have been used since the 1930's and today four main types are available. All these CM are derived from one original structure: the 2,4,6 triiodobenzoic acid with the substituents in positions 1,2 and 5 as a carboxylic group or amides. According to the nature of the substituents and the number of aromatic rings, the four different types of CM can be identified. Three of the four types of CM are hyperosmolar, some of the ionic CM contain meglumine and all CM contain calcium disodium EDTA. To fulfil their role in host defence, circulatory PMN must adhere to endothelium of capillaries and venules adjacent to the **inflammatory** locus, migrate through the vessel wall to the area of **inflammation**, phagocytose opsonized bacteria, kill **ingested** organisms and, finally, inactivate their own toxic products to prevent damage to normal tissue. CM should be biologically inert, but many physiological and pathophysiological effects have been described. This review deals with the present knowledge about the influence of CM on PMN. This thesis presents results of the effects of the four main types of CM on PMN exocytosis of elastase and **lactoferrin**, adherence to nylon fibers, chemotaxis under agarose and phagocytosis of latex particles, as well after in vitro exposure of CM to PMN and after intravascular injection of CM. After in vitro exposure of CM to whole blood, a dose-dependent fall in **lactoferrin** and elastase concentration was observed, statistically significant for diatrizoate and ioxaglate at high concentrations. I.v. injection of iohexol or ioxaglate resulted in small, although statistical, decreases in **lactoferrin** concentration in plasma. No differences between the CM groups were seen. PMN adherence to nylon fibers after incubation of CM with whole blood or isolated PMNs was inhibited. The most inhibitive agents were the ionic CM diatrizoate and ioxaglate. The meglumine ion was found to contribute to the inhibitive effect of diatrizoate upon adherence. Following i.v. injection of iohexol or ioxaglate, increased numbers of PMNs, in combination with decreased adherence, were noted with ioxaglate, and the opposite with iohexol. Immediately after arteriography with iohexol and ioxaglate, a small increase of PMN count, in combination with decreased adherence, could be seen. An inhibition of adherence will result in a shift from the marginal to the circulatory pool of PMNs and thus an increase in PMN count. Although statistically significant the changes were minor. A pronounced increase in PMN count was seen 2-5 hours after arteriography in combination with a decrease in adherence. These changes may be due to a release of glucocorticoids from the adrenals in response to the procedure and/or the injection of CM. CMs do not act as chemoattractants. However, when CM are added to the chemoattractant N-fMLP in the under agarose assay, the number of PMNs migrating (density) was lowered, while the distance migrated by the leading front was not affected except for diatrizoate that almost abolished migration. When diatrizoate was added to PMNs, a dose-dependent inhibition was observed. Following i.v. injection of CM, no changes in PMN chemotaxis or changes in the chemoattractive potential of serum could be demonstrated compared to the baseline levels. The ability of PMNs to **ingest** latex particles after incubation with CM was inhibited in a dose-dependent way. The most inhibitive agents were diatrizoate and ioxaglate. A solution containing the same amount of disodium calcium EDTA as the CM solutions inhibited phagocytosis significantly, although less than the CM solution. Improved phagocytosis was observed in hyperosmolar environments due to NaCl or mannitol at osmolarities higher than 369 mOsm. I.v. injection of ioxaglate or iohexol inhibited the phagocytosis of latex particles by PMNs. The impairment was most pronounced immediately after the injection, and had almost returned to ba

L58 ANSWER 15 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

Searched by: Mary Hale 571-272-2507 REM 1D86

ACCESSION NUMBER: 1996:532490 BIOSIS
DOCUMENT NUMBER: PREV199699254846
TITLE: Oral administration of bovine **lactoferrin** for treatment of intractable stomatitis in feline immunodeficiency virus (FIV)-positive and FIV-negative cats.
AUTHOR(S): Sato, Reeko [Reprint author]; Inanami, Osamu; Tanaka, Yukiko [Reprint author]; Takase, Mitsunori; Naito, Yoshihisa [Reprint author]
CORPORATE SOURCE: Dep. Veterinary Internal Med., Fac. Agric., Iwate Univ., Morioka, 020, Japan
SOURCE: American Journal of Veterinary Research, (1996) Vol. 57, No. 10, pp. 1443-1446.
CODEN: AJVRAH. ISSN: 0002-9645.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Nov 1996
Last Updated on STN: 22 Nov 1996

AB Objective: To study the effects of oral administration of bovine **lactoferrin** (LF) on intractable stomatitis in feline immunodeficiency virus (FIV)-positive and FIV-negative cats, and phagocytosis of **neutrophils** in healthy and ill cats, simultaneously. Animals: 7 ill cats with diagnosis of intractable stomatitis (4 FIV positive and 3 FIV negative) and 7 healthy, FIV-negative cats. Procedure: LF (40 mg/kg of body weight) was applied topically to the oral mucosa of cats with intractable stomatitis daily for 14 days and improvement of clinical signs of disease (pain-related response, salivation, appetite, and oral **inflammation**), expressed by scoring from 1 to 4, were evaluated. Assay of **neutrophil** phagocytosis was examined before and 2 weeks after starting LF treatment, using nonopsonized hydrophilic polymer particles (2 mu-m). Results: Oral administration of LF improved intractable stomatitis in all 4 respects. Phagocytic activity of **neutrophils** increased after LF treatment. This effect was observed in healthy and ill (FIV positive and FIV negative) cats. Conclusion and Clinical Relevance: Oral administration of LF improved intractable stomatitis and concurrently enhanced the host defense system. Topical application of LF to oral mucous membrane is useful as a treatment for intractable stomatitis even in FIV-positive cats.

L58 ANSWER 16 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1995:281246 BIOSIS
DOCUMENT NUMBER: PREV199598295546
TITLE: Fecal **lactoferrin** as a marker for disease activity in **inflammatory** bowel disease: Comparison with other **neutrophil** granule-derived proteins.
AUTHOR(S): Sugi, K. [Reprint author]; Saitoh, O.; Matsuse, R.; Uchida, K.; Nakagawa, K.; Yoshizumi, M.; Takada, K.; Hirata, I.; Katsu, K.
CORPORATE SOURCE: 2nd Dep. Int. Med., Osaka Med. Coll., Osaka, Japan
SOURCE: Gastroenterology, (1995) Vol. 108, No. 4 SUPPL., pp. A924.
Meeting Info.: 95th Annual Meeting of the American Gastroenterological Association and Digestive Disease Week. San Diego, California, USA. May 14-17, 1995.
CODEN: GASTAB. ISSN: 0016-5085.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Jul 1995
Last Updated on STN: 5 Jul 1995

Searched by: Mary Hale 571-272-2507 REM 1D86

L58 ANSWER 17 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1996:22064 BIOSIS
DOCUMENT NUMBER: PREV199698594199
TITLE: Correlation of **lactoferrin** with neutrophilic **inflammation** in **body fluids**.
AUTHOR(S): Martins, Clovis A. P.; Fonteles, Maria G.; Barrett, Leah J.; Guerrant, Richard L. [Reprint author]
CORPORATE SOURCE: Box 485, Div. Geographic and Int. Med., Univ. Va. Sch. Med., Charlottesville, VA 22908, USA
SOURCE: Clinical and Diagnostic Laboratory Immunology, (1995) Vol. 2, No. 6, pp. 763-765.
ISSN: 1071-412X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Jan 1996
Last Updated on STN: 12 Jan 1996

AB We have reported that **lactoferrin**, a 77-kDa iron-binding glycoprotein found in secondary **neutrophil** granules, provides a useful marker of fecal leukocytes in fecal specimens from patients with **inflammatory** diarrhea (R. L. Guerrant, V. Araujo, E. Soares, K. Kotloff, A. A. M. Lima, W. H. Cooper, and A. G. Lee, J. Clin. Microbiol. 30:1238-1242, 1992). In order to determine the usefulness of this marker of neutrophilic **inflammation** in different **body fluids**, we examined blood, gingival swabs, sputum, and saliva using **antilactoferrin** antibodies (**lactoferrin** latex agglutination (LFLA)). LFLA titers in whole blood samples were ltoreq 1:4 in all eight samples from patients with neutropenia (absolute **neutrophil** count (ANC) = lt 150 polymorphonuclear cells (PMNs) per mu-l), ltoreq 1:8 in samples from 13 individuals with moderate leukocyte counts (ANC = 150 to 8,000), and 1:8 to 1:32 in samples from six patients with neutrophilia (ANC gt 8,000). While the overlap precludes a useful role in the identification of neutropenia, these data confirm that **lactoferrin** titers of gt 1:100 indeed indicate **inflammation** in fluid specimens. On quantitative elution of **lactoferrin** from gingival swabs, all 7 patients with dental plaque had titers of 1:200 to 1:400; 9 of 12 patients with clinical gingivitis had LFLA titers of 1:200 to 1:1,600, while all 7 individuals with healthy gums and teeth and 4 edentulous patients had LFLA titers of ltoreq 1:100. Eight purulent sputum samples had titers of gtoreq 1:400 (7 were 1:1,600) while 11 normal saliva samples showed titers of ltoreq 1:100. **Lactoferrin** titers in sputum, gingival swabs, and whole blood correlate with the presence of **neutrophils** or **inflammation** in these specimens and may offer a convenient rapid test for **inflammatory** processes.

L58 ANSWER 18 OF 33 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 95204853 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7897158
TITLE: Products of arachidonic acid metabolism and the effects of cyclooxygenase inhibition on ongoing cutaneous allergic reactions in human beings.
AUTHOR: Atkins P C; Zweiman B; Littman B; Presti C; von Allmen C; Moskovitz A; Eskra J D
CORPORATE SOURCE: Department of Medicine, University of Pennsylvania School of Medicine, Philadelphia 19104-6057.
CONTRACT NUMBER: AI-14332 (NIAID)
SOURCE: Journal of allergy and clinical immunology, (1995 Mar) 95 (3) 742-7.
Journal code: 1275002. ISSN: 0091-6749.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)

Searched by: Mary Hale 571-272-2507 REM 1D86

(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199504
ENTRY DATE: Entered STN: 19950504
Last Updated on STN: 19950504
Entered Medline: 19950425

AB BACKGROUND: There have been conflicting reports about the effects of inhibition of arachidonic acid metabolism on early- and late-phase cutaneous reactions. We re-examined this question with a unique nonsteroidal antiinflammatory drug, tenidap sodium. Tenidap sodium has been demonstrated in in vitro studies to inhibit cyclooxygenase, lipoxygenase, and cytokine production (interleukin-1, interleukin-6, **tumor necrosis factor-alpha**).
METHODS: In a double-blind, randomized, crossover study, seven pollen-sensitive subjects **ingested** tenidap (120 mg, by mouth, daily) and placebo for 9 days with a 3-week washout period between treatments. On the eighth day they underwent allergen skin testing, measurable for up to 12 hours, and on the ninth day they underwent 5-hour skin chamber exposures to allergen and buffer. Chamber fluids were analyzed for cellular content, **neutrophil** granule protein release, cyclooxygenase and lipoxygenase arachidonic acid metabolites, histamine, and tryptase. RESULTS: Tenidap did significantly inhibit cyclooxygenase metabolites at both antigen and buffer sites but had no effect on histamine, tryptase, lipoxygenase metabolites, or granulocyte infiltration. **Neutrophil** granule release of **lactoferrin** was lower at the antigen site during tenidap administration, but there was no reduction of elastase release. Prostaglandin E2 and leukotriene E4 increased significantly at antigen sites compared with buffer sites during placebo administration and were the most prominent arachidonic acid metabolites detected. CONCLUSION: Tenidap, despite inhibiting cyclooxygenase release at antigen sites, had no effect on skin test responses to antigen or on antigen-induced mediator release or granulocyte infiltration. We conclude that cyclooxygenase metabolites are not important in the development of an allergic cutaneous **inflammatory** response.

L58 ANSWER 19 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1995:272389 BIOSIS
DOCUMENT NUMBER: PREV199598286689
TITLE: Prednisone inhibits leukocyte granule secretion into the asthmatic airway.
AUTHOR(S): Joseph, B. Z.; Beam, R.; Martin, R. J.; Borish, L. [Reprint author]
CORPORATE SOURCE: Dep. Med., 1400 Jackson Street, Denver, CO 80206, USA
SOURCE: International Journal of Immunopathology and Pharmacology, (1995) Vol. 8, No. 1, pp. 23-30.
ISSN: 0394-6320.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jun 1995
Last Updated on STN: 26 Jun 1995

AB Asthmatic subjects **ingested** prednisone (50 mg) or a placebo one week apart at 8 pm followed by bronchoalveolar lavage (BAL) at 4 am on each occasion. For subjects **ingesting** the prednisone at 8 pm, the total BAL fluid cell counts at 4 am were not significantly different with either the placebo or prednisone. After cellular pellets were removed, assays for **lactoferrin** (**neutrophil** secondary granule marker), beta-glucuronidase (present in eosinophils, macrophages, and **neutrophil** primary granules), lysozyme (**neutrophil** primary and secondary granules), and major basic protein (MBP; eosinophil marker) were performed. **Lactoferrin** concentrations were 82 +- 9

Searched by: Mary Hale 571-272-2507 REM 1D86

ng/ml BAL fluid on placebo and 62 +- 16 ng/ml on prednisone nights (p=N.S.). beta-glucuronidase was 11+-3 mg/ml on placebo and 3+-1 on prednisone nights (p lt .05) whereas lysozyme was 12+-2 and 5+-1 on placebo and prednisone nights, respectively (p lt .02). A semiquantitative ELISA for MBP revealed a mean 51.2+-10.2% suppression of MBP secretion in the subjects who **ingested** prednisone compared to placebo (p=.03). These observations demonstrate that pharmacological concentrations of prednisone prevent release of **neutrophil** and eosinophil granule contents in vivo while having no effect on the **neutrophil** secondary granule marker **lactoferrin**. Thus, prednisone suppresses cell function 8 hrs after it is administered while cell counts remained unchanged.

L58 ANSWER 20 OF 33 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 96234418 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8699856
TITLE: Cytokines, phagocytes, and pentoxifylline.
AUTHOR: Mandell G L
CORPORATE SOURCE: Division of Infectious Disease, University of Virginia Health Sciences Center, Charlottesville 22908, USA.
SOURCE: Journal of cardiovascular pharmacology, (1995) 25 Suppl 2 S20-2. Ref: 7
Journal code: 7902492. ISSN: 0160-2446.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19960912
Last Updated on STN: 19960912
Entered Medline: 19960905

AB Phagocytic cells, such as polymorphonuclear **neutrophils**, monocytes, and macrophages, are essential for defense against infection caused by a variety of microorganisms. The mechanisms used by these cells to destroy microbes comprise a potent oxidative armamentarium including superoxide, hydrogen peroxide, and hypochlorous acid. In addition, granule contents such as proteolytic enzymes, lysozyme, **lactoferrin**, and myeloperoxidase are released into the phagosome to destroy **ingested** microorganisms. **Inflammatory** cytokines, such as tumor necrosis factor (TNF), interleukin-1 (IL-1), and IL-6, enhance the phagocytic and microbicidal activity of the cells and increase their stickiness. It has been demonstrated in a variety of animal and clinical studies that activated phagocytes can damage the host they are designed to protect, using the mechanisms described above. Alkylxanthines, including pentoxifylline, are potent inhibitors of this **inflammatory** damage by two major actions: (a) reduction of the production of **inflammatory** cytokines (especially TNF) by phagocytes stimulated with a variety of microbial products (e.g., endotoxin); and (b) reversal of the effect of these cytokines on phagocytes. Thus, pentoxifylline counteracts the following effects of **inflammatory** cytokines on phagocytes: increased adherence, shape change resulting in larger size and rigidity, increased oxidative burst, priming for an enhanced oxidative burst, increased degranulation, and decreased chemotactic movement. In addition, these activities synergize with the normal anti-**inflammatory** mediator adenosine. Alkylxanthines have the potential to be effective therapy for conditions in which **inflammatory** cytokines and phagocytes cause damage, including the sepsis syndrome, ARDS, AIDS, and arthritis.

L58 ANSWER 21 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

Searched by: Mary Hale 571-272-2507 REM 1D86

ACCESSION NUMBER: 1994:315676 BIOSIS
DOCUMENT NUMBER: PREV199497328676
TITLE: P-selectin-dependent leukocyte recruitment and intestinal mucosal injury induced by **lactoferrin**.
AUTHOR(S): Kurose, Iwao; Yamada, Tamaki; Wolf, Robert; Granger, D. Neil [Reprint author]
CORPORATE SOURCE: Dep. Physiol., LSU Med. Cent., 1501 Kings Highway, P.O. Box 33932, Shreveport, LA 71130-3932, USA
SOURCE: Journal of Leukocyte Biology, (1994) Vol. 55, No. 6, pp. 771-777.
CODEN: JLBIE7. ISSN: 0741-5400.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jul 1994
Last Updated on STN: 26 Jul 1994

AB Plasma concentrations of **lactoferrin** relevant to an **inflammatory** response are known to elicit leukocyte-endothelial cell adhesion in mesenteric venules. The objectives of this study were (1) to determine whether exogenously administered **lactoferrin** causes microvascular and mucosal injury in rat intestine and (2) to assess the contribution of adherent leukocytes to a **lactoferrin** -mediated injury process. Mucosal myeloperoxidase (MPO) activity and vascular protein clearance were monitored in the distal intestine of male Sprague-Dawley rats. Macroscopic erosive lesions of the mucosa and increases in mucosal MPO and intestinal vascular protein were observed 2 h following the **lactoferrin** infusion, results consistent with granulocyte accumulation and microvascular protein leakage. These **lactoferrin**-induced alterations were significantly attenuated in animals pretreated with a monoclonal antibody (mAb) directed against P-selectin but not by an E-selectin-specific mAb. In another series of experiments, leukocyte adherence/emigration and leakage of fluorescein isothiocyanate (FITC)-labeled **albumin** were measured in rat mesenteric venules using intravital video microscopy. **Lactoferrin** elicited increases in both leukocyte adhesion/emigration and **albumin** extravasation, which were attenuated by mAbs directed against P-selectin but not E-selectin. These observations indicate that (1) the **lactoferrin** released by activated **neutrophils** may lead to significant microvascular and mucosal injury or dysfunction and (2) the **lactoferrin**-induced injury is related to P-selectin-mediated adhesion of leukocytes to microvascular endothelium. Our results raise the possibility that **neutrophil**-derived **lactoferrin** contributes to the **inflammatory** response by promoting further granulocyte accumulation and activation and that mAbs to P-selectin may be therapeutically beneficial in **inflammatory** disorders.

L58 ANSWER 22 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 4
ACCESSION NUMBER: 1994:319628 BIOSIS
DOCUMENT NUMBER: PREV199497332628
TITLE: Effect of **ingested** pentoxifylline on the ex vivo **neutrophil** function of patients with varicose leg ulcers.
AUTHOR(S): Crouch, S. P. M. [Reprint author]; Saihan, E. M.; Fletcher, J. [Reprint author]
CORPORATE SOURCE: Med. Res. Cent., City Hosp., Nottingham, Nottingham, UK
SOURCE: Clinical Hemorheology, (1994) Vol. 14, No. 3, pp. 379-392.
CODEN: CLHEDF. ISSN: 0271-5198.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jul 1994
Last Updated on STN: 27 Jul 1994

Searched by: Mary Hale 571-272-2507 REM 1D86

AB Polymorphonuclear leukocytes (PMN) appear to play a role in the pathogenesis of leg ulceration through tissue damage occurring as a result of these cells being trapped within the capillaries in anoxic tissue. The aim of this study was to determine whether **ingestion** of a 400mg slow release tablet of pentoxifylline (PTOX) would cause a reduction in the ex vivo responses of PMN isolated from patients with varicose leg ulcers. Superoxide anion production, as measured by lucigenin-enhanced chemiluminescence was significantly reduced at 2 and 4 hours post-**ingestion** in response to stimulation by formylmethionylleucylphenylalanine (FMLP) and C5a des arg in zymosan activated serum (ZAS). The response to FMLP was reduced by 39% ($p=0.014$) at 2 hours and by 32% ($p=0.029$) at 4 hours. The response to ZAS was reduced by 52% at 2 hours ($p=0.007$) and 50% at 4 hours ($p=0.0104$). Upregulation of the adhesion molecule CD11b in response to FMLP and ZAS was also significantly reduced in the patient group at 2 ($p=0.010$ for both stimuli) and 4 hours after **ingestion** (FMLP, $p=0.0212$; ZAS, $p=0.0150$), although the unstimulated expression of this molecule remained constant. There were no significant differences in the PMN responses observed when data for the patients was compared with the control group. These results suggest that the previous in vitro and ex vivo observations with PTOX on PMN from normal subjects can be reproduced with cells from patients suffering with varicose leg ulcers. PTOX may reduce recruitment and activation of further cells into the **inflammatory** foci and thus help prevent exacerbations of **inflammation**.

L58 ANSWER 23 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1994:500935 BIOSIS
DOCUMENT NUMBER: PREV199497513935
TITLE: Pathogenesis of mastitis.
AUTHOR(S): Bozic, Tatjana; Knezevic, Milijana
CORPORATE SOURCE: Vet. Fak., Beograd, Yugoslavia
SOURCE: Veterinarski Glasnik, (1994) Vol. 48, No. 3-4, pp. 165-172. CODEN: VEGLAI. ISSN: 0350-2457.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: Serbo-Croatian
ENTRY DATE: Entered STN: 28 Nov 1994
Last Updated on STN: 28 Nov 1994

AB Mastitis appears frequently in domestic animals, especially in cows, since they are exposed to prolonged lactation-related stress the longest. Mastitis appears mostly as a consequence of selective adherence of different bacteria to fibronectin of the canalicular system of the mammary gland. Mycoplasmas and fungi are also mentioned as possible pathogenic elements. Galactogenic infection has a vast importance and is widely accepted as the most important pathway for the entry of micro-organisms. A hematogenic reaction is relatively rare and appears in connection with E. coli. In addition to this type of infection, infection through the skin is also possible, either percutaneously or through open wounds. The changes which characterize **inflammations** of the mammary gland are directed by substances which are either released from mastocytes, **neutrophils**, macrophages and fibroblasts or are synthesized de novo. The mammary gland, like other organs (the lungs, intestine, urinary and genital apparatus) contains numerous defence organisms, primarily phagocytosis. **Neutrophils** of the mammary gland have an increased capacity for phagocytosis because of **ingestion** of fatty substances, greater than blood granulocytes, helped also by the local immunoglobulins, especially IgG2, IgM and IgA. Moreover, the opsonizing effect of milk, the importance of **lactoferrin** from lysosomes regarding certain bacteria, the increased level of the lactoperoxidase-thiocyanate-hydrogen-peroxide system, are also among the factors essential to the defence mechanism of the udder against different pathogenic factors. Keratin, which synthesizes glandular epithelium, is

one of the morphological factors of resistance to different forms of infection of the canal system of the mammary gland.

L58 ANSWER 24 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1994:291967 BIOSIS
DOCUMENT NUMBER: PREV199497304967
TITLE: Correlation of **lactoferrin** with neutrophilic **inflammation** in **body fluids**.
AUTHOR(S): Martins, C. A. P. [Reprint author]; Fonteles, M. G.; Guerrant, R. L.
CORPORATE SOURCE: Unidade de Pesquisas Clinicas, Universidade Federal do Ceara, Fortaleza, Brazil
SOURCE: Clinical Research, (1994) Vol. 42, No. 2, pp. 151A. Meeting Info.: Meeting of the American Federation for Clinical Research. Baltimore, Maryland, USA. April 29-May 2, 1994.
CODEN: CLREAS. ISSN: 0009-9279.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jun 1994
Last Updated on STN: 30 Jun 1994

L58 ANSWER 25 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1993:353888 BIOSIS
DOCUMENT NUMBER: PREV199345037313
TITLE: **Lactoferrin**-induced microvascular and mucosal injury in rat intestine: Role of leukocytes.
AUTHOR(S): Kurose, I. [Reprint author]; Wolf, R.; Granger, D. N.
CORPORATE SOURCE: Dep. Physiol., LSU Med. Cent., Shreveport, LA 71130, USA
SOURCE: Gastroenterology, (1993) Vol. 104, No. 4 SUPPL., pp. A729. Meeting Info.: 94th Annual Meeting of the American Gastroenterological Association. Boston, Massachusetts, USA. May 15-21, 1993.
CODEN: GASTAB. ISSN: 0016-5085.
DOCUMENT TYPE: Conference; (Meeting)
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jul 1993
Last Updated on STN: 31 Jul 1993

L58 ANSWER 26 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1993:455002 BIOSIS
DOCUMENT NUMBER: PREV199396099902
TITLE: Role of T cells in the pathogenesis of periapical lesions: A preliminary report.
AUTHOR(S): Wallstrom, John B. [Reprint author]; Torabinejad, Mahmoud; Kettering, James; McMillan, Paul
CORPORATE SOURCE: 17118 S.E. 328th St., Auburn, WA 98002, USA
SOURCE: Oral Surgery Oral Medicine Oral Pathology, (1993) Vol. 76, No. 2, pp. 213-218.
CODEN: OSOMAE. ISSN: 0030-4220.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Oct 1993
Last Updated on STN: 5 Oct 1993
AB The pulps of mandibular molars of 15 athymic and 15 conventional rats were surgically exposed and left open to their oral flora. Each group was divided into three subgroups of five animals each. The rats were killed after their pulps were exposed for 2, 4, or 8 weeks. After fixing, decalcifying, and embedding, the specimens were sectioned and stained with hemotoxylin and eosin. They were then examined under a microscopic grid

Searched by: Mary Hale 571-272-2507 REM 1D86

and quantified by percentages of surface areas of bone, connective tissue, bone marrow, intrabony spaces, periapical lesions, and numbers of osteoclasts, with the use of a Data Voice computerized data collection and analysis system. Statistical analysis showed no significant difference between periapical tissue responses of the conventional and athymic groups. The results indicate that the pathogenesis of periapical lesions is a multifactorial phenomenon and is not totally dependent on the presence of T-cell lymphocytes.

L58 ANSWER 27 OF 33 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 93014162 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1356929
TITLE: Effect of **ingested** pentoxifylline on **neutrophil** superoxide anion production.
AUTHOR: Crouch S P; Fletcher J
CORPORATE SOURCE: Medical Research Centre, City Hospital, Nottingham, United Kingdom.
SOURCE: Infection and immunity, (1992 Nov) 60 (11) 4504-9. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199211
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19950206
Entered Medline: 19921125

AB Superoxide and other oxygen radicals produced by activated polymorphonuclear leukocytes (PMN) may be important causes of tissue damage in a number of **inflammatory** conditions. Therefore, a drug which suppresses PMN responses in vivo is potentially important. In vitro, pentoxifylline (PTOX) inhibits superoxide anion production when PMN are stimulated with an activated complement component (C5a Des Arg) or formyl peptides but only at concentrations not achieved in the circulation. The aim of this study was to determine whether PTOX has an effect on PMN responses in vivo. Superoxide anion production, monitored by lucigenin-enhanced chemiluminescence, was inhibited by 40.5% +/- 8.0% ($n = 8$, $P < 0.009$) for C5a Des Arg and 47.7% +/- 9.6% ($n = 8$, $P < 0.009$) for formyl-methionylleucylphenylalanine stimulation 1.5 h after **ingestion** of 400 mg of PTOX in a slow-release tablet, with some inhibitory effects persisting at 5 h. There was a strong correlation between reduced PMN response to activated complement and plasma concentrations of three PTOX metabolites ($P < 0.05$), but not with plasma concentrations of the parent drug. In vitro investigations with each of the four methylxanthines showed two of these metabolites to be most effective at reducing PMN respiratory burst activity, **lactoferrin** release, and the expression of CD11b and CD18 molecules. Furthermore, this in vitro inhibitory activity was achieved at concentrations of metabolites achievable in vivo. The results suggest that PTOX reduces oxygen radical production and protects against unwanted tissue damage in vivo by the action of its metabolites.

L58 ANSWER 28 OF 33 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 90149170 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2154270
TITLE: Release of iron from phagocytosed Escherichia coli and uptake by **neutrophil lactoferrin**.
AUTHOR: Molloy A L; Winterbourn C C
CORPORATE SOURCE: Department of Pathology, School of Medicine, Christchurch Hospital, New Zealand.
SOURCE: Blood, (1990 Feb 15) 75 (4) 984-9. Journal code: 7603509. ISSN: 0006-4971.

Searched by: Mary Hale 571-272-2507 REM 1D86

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199003
ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19970203
Entered Medline: 19900320

AB Escherichia coli were labeled with 59Fe and then either treated with myeloperoxidase, H2O2, and chloride or opsonized and mixed with human **neutrophils**. The myeloperoxidase system at pH 7.4 caused release of most of the bacterial 59Fe. A similar result has been obtained by Rosen and Klebanoff (J Biol Chem 257:13731, 1982) but at pH 5. Iron release at pH 7.4 did not require the presence of a chelator, and the majority passed through a 10,000 relative molecular mass cut-off ultrafiltration membrane. When iron-poor **lactoferrin** was present during incubation with myeloperoxidase, 88% of the released 59Fe was precipitated with anti-**lactoferrin** antiserum, indicating that it was **lactoferrin**-bound. When the bacteria were mixed with **neutrophils** in a 10:1 ratio, approximately 50% were phagocytosed. About 40% of the 59Fe was released from the **ingested** bacteria over a 40-minute period. Initially, most remained associated with the **neutrophil** phagosomes, but with time, there was gradual transfer of some of the iron to the medium. Using anti-**lactoferrin** antiserum, 50% to 60% of phagosomal iron and 64% to 71% of iron in the medium was shown to be bound to **lactoferrin**. Thus, iron is released from phagocytosed E coli. Most becomes bound to **lactoferrin**, and some of this is released into the surroundings of the **neutrophils**. This suggests that **neutrophil lactoferrin** may function to trap iron from **ingested** microorganisms, enabling its removal from sites of **inflammation**. This may prevent iron from catalyzing undesirable oxidative reactions, as well as making it unavailable for growth of microorganisms that survive the killing process.

L58 ANSWER 29 OF 33 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 89008870 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3049672
TITLE: Studies on the molecular mechanisms of human Fc receptor-mediated phagocytosis. Amplification of **ingestion** is dependent on the generation of reactive oxygen metabolites and is deficient in polymorphonuclear leukocytes from patients with chronic granulomatous disease.
AUTHOR: Gresham H D; McGarr J A; Shackelford P G; Brown E J
CORPORATE SOURCE: Department of Medicine, Washington University School of Medicine, St. Louis, Missouri 63110.
CONTRACT NUMBER: AI-19350 (NIAID)
AI-23790 (NIAID)
GM-38330 (NIGMS)
SOURCE: Journal of clinical investigation, (1988 Oct) 82 (4) 1192-201.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198811
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19990129
Entered Medline: 19881115

AB Human PMN and monocytes both possess a mechanism for amplifying Fc

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receptor-mediated phagocytic function, which is dependent on activation of the respiratory burst. The pathway for augmentation of phagocytosis requires superoxide anion, hydrogen peroxide, and **lactoferrin** and is independent of the hydrogen peroxide-MPO-halide system. In neither cell type is this mechanism induced upon exposure to the opsonized target. PMN require an additional signal for stimulation of the respiratory burst; this is not true of monocytes. On the other hand, monocytes require an exogenous source of **lactoferrin** in order to activate this pathway for enhanced **ingestion**. The dependence of this pathway for both PMN and monocytes on superoxide anion, hydrogen peroxide, and cell-bound **lactoferrin** is consistent with a role for locally generated reactive oxygen metabolites, possibly hydroxyl radicals, in phagocytosis amplification. Patients with chronic granulomatous disease, who are genetically deficient in the ability to activate the respiratory burst, are unable to amplify Fc receptor-mediated phagocytosis. Thus, these patients may have a previously unrecognized defect in the recruitment of phagocytic function at **inflammatory** sites.

L58 ANSWER 30 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 8

ACCESSION NUMBER: 1986:359166 BIOSIS
DOCUMENT NUMBER: PREV198682063640; BA82:63640
TITLE: CONTRIBUTIONS OF THE MAC-1 GLYCOPROTEIN FAMILY TO ADHERENCE-DEPENDENT GRANULOCYTE FUNCTIONS STRUCTURE-FUNCTION ASSESSMENTS EMPLOYING SUBUNIT-SPECIFIC MONOCLONAL ANTIBODIES.
AUTHOR(S): ANDERSON D C [Reprint author]; MILLER L J; SCHMALISTIEG F C; ROTHLEIN R; SPRINGER T A
CORPORATE SOURCE: TEX CHILDREN'S HOSP, LEUKOCYTE BIOL SECT, HOUSTON, TEX 77030, USA
SOURCE: Journal of Immunology, (1986) Vol. 137, No. 1, pp. 15-27. CODEN: JOIMA3. ISSN: 0022-1767.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 6 Sep 1986
Last Updated on STN: 6 Sep 1986

AB MAb directed at the α-subunits of Mac-1 (αM), LFA-1 (αL), p150,95 (αX), or their common β-subunit were used to characterize the contributions of the Mac-1 glycoprotein family to granulocyte adherence reactions. Inhibitory effects of these MAb in incubation experiments with normal granulocytes indicated distinct adhesive contributions of each subunit. Significantly greater adherence, and inhibition of adherence by anti αM, αX, and β MAb, was observed under chemotactic conditions designed to "up-regulate" the surface expression of the αM β and αX β complexes. Adherence to protein-coated glass and binding of **albumin**-coated latex beads were significantly inhibited by anti-β > anti-αM (OKM-10, M1/70, LM2/1.6 and OKM-1) > antiαX > anti-αL MAb, but no effects of anti-HLA, AB, or anti-CR-1 MAb were evident. A similar rank order of inhibition was observed in granulocyte aggregation assays in response to C5a, PMA, or f-Met-Leu-Phe. Significant inhibition of directed migration by anti-β or anti-αM (OKM-1 or OKM-10) MAb was observed in subagarose but not Boyden chemotaxis assays; inhibition was dependent on a continuous cell exposure to anti-Mac-1α or β during the assay, suggesting that a continuum of new Mac-1 expression is required for directed translocation. Phagocytosis of Oil-Red-O paraffin or zymosan selectively opsonized with C3-derived ligands was significantly inhibited by anti-αM MAb (OKM-10 > LM2/1.6 > M1/70 > OKM-1) or by combinations of anti-αM + anti-CR-1 MAb, but only minimal inhibitory effect of anti-β MAb and no effects of anti-αL or anti-αX MAb were seen. Similarly, complement-dependent

phagocytosis-associated **lactoferrin** release, **ingestion** and intracellular killing of Staphylococcus aureus 502A, and binding of iC3b-opsonized SRBC, were significantly inhibited by anti-αM (OKM-10, M1/70) or combinations of anti-αM + anti-CR-1 MAb, but not by anti-β, αL, or αX MAb. Notably, none of the anti-Mac-1 MAB demonstrated inhibitory effects in assays of adherence-independent functions including shape change, specific f-Met-Leu-3H-Phe binding, O2- generation, chemiluminescence evolution, or **lactoferrin** release in response to PMA. These studies indicate that MAb directed at individual subunits or combinations of subunits of the Mac-1 glycoprotein family can be employed in blocking experiments to elicit function abnormalities of granulocytes similiar to those recognized in patients with a genetic deficiency of Mac-1, LFA-1, and p150,95. Thus, our findings provide additional evidence for an important physiologic role of this leukocyte glycoprotein family in the **inflammatory** response.

L58 ANSWER 31 OF 33 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1982:223252 BIOSIS
DOCUMENT NUMBER: PREV198273083236; BA73:83236
TITLE: **LACTOFERRIN** INTERACTS WITH DNA A PREFERENTIAL REACTIVITY WITH DOUBLE STRANDED DNA AND DISSOCIATION OF DNA ANTI DNA COMPLEXES.
AUTHOR(S): BENNETT R M [Reprint author]; DAVIS J
CORPORATE SOURCE: DEP MED, OREG HEALTH SCI UNIV, 3181 SW SAM JACKSON PARK ROAD, PORTLAND, OREG 97201, USA
SOURCE: Journal of Laboratory and Clinical Medicine, (1982) Vol. 99, No. 1, pp. 127-138.
CODEN: JLCMAK. ISSN: 0022-2143.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB LF [**lactoferrin**] bound to DNA as assessed by immunofluorescence studies on mouse liver cell nuclei, affinity chromatography of DNA on immobilized LF and gel chromatography of an LF-DNA reaction mixture. LF immobilized on Sepharose 4-B was reacted with 125I-labeled DNA in both its double-stranded [ds] and single-stranded [ss] configurations; dsDNA eluted with a 0.69 M NaCl buffer, whereas ssDNA eluted with a 0.25 M NaCl buffer. Additional evidence for a preferential reactivity with dsDNA was provided by the enzymatic treatment of preformed dsDNA-LF and ssDNA-LF complexes with S1 endonuclease, and DNAse 1.sbd.DNAse digestion alone liberated free LF. The interaction of LF with DNA partially inhibited the binding of anti-DNA antibodies from patients with SLE [systemic lupus erythematosus] as assayed in a standard Farr assay. DNA-anti-DNA (labeled with 125I-IgG) complexes could be dispersed in vitro by the addition of LF. The release of LF by **neutrophils** chemotactically attracted to DNA-anti-DNA complexes may act as a feedback loop to modulate the **inflammatory** response in SLE.

L58 ANSWER 32 OF 33 MEDLINE on STN
ACCESSION NUMBER: 79172248 MEDLINE
DOCUMENT NUMBER: PubMed ID: 35468
TITLE: **Neutrophil** function and host resistance.
AUTHOR: Zakhireh B; Block L H; Root R K
SOURCE: Infection, (1979) 7 (2) 88-98.
Journal code: 0365307. ISSN: 0300-8126.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197907
ENTRY DATE: Entered STN: 19900315

Searched by: Mary Hale 571-272-2507 REM 1D86

Last Updated on STN: 20030222
Entered Medline: 19790725

AB The part played by the phagocytic cells against invading pathogens has been known since the work of Metchnikoff nearly a century ago. This review deals primarily with the role of the neutrophilic polymorphonuclear leukocyte in host defense against microbial infections. The overall function of these cells in protection from infection is dependent on a number of steps. First, an adequate number of functionally mature **neutrophils** have to be produced and released into the circulation by the bone marrow. Cells must circulate normally and be capable of adhering to capillary and venule walls overlying **inflammatory** sites. The next step involves the exit of phagocytes from the blood stream through the capillary wall and emigration into the tissues to establish contact with the invading pathogens. This process is accomplished by the locomotive characteristics of these cells and chemotaxis. Most organisms must then be phagocytized to be killed. Two discrete phases are involved in phagocytosis; the "recognition" and attachment phase followed by the **ingestion** phase. After phagocytosis a series of coordinated morphologic and biochemical events are set into motion which leads to eventual death and lysis of the **ingested** microbes. A variety of antimicrobial mechanisms are involved in this final step and indicate that these cells have an appreciable reserve capacity if one mechanism is impaired. Recent evidence which clarifies mechanisms involved in all these stages is discussed.

L58 ANSWER 33 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 1975:71148 HCAPLUS
DOCUMENT NUMBER: 82:71148
TITLE: Involvement of **lactoferrin** in the hyposideremia of acute **inflammation**
AUTHOR(S): Van Snick, Jacques L.; Masson, Pierre L.; Heremans, Joseph F.
CORPORATE SOURCE: Dep. Exp. Med., Univ. Louvain, Brussels, Belg.
SOURCE: Journal of Experimental Medicine (1974), 140(4), 1068-84
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Exptl. work on rats showed that the hyposideremia of **inflammation** is based on a 3-step mechanism involving **lactoferrin** (I), the iron-binding protein from the specific granules of **neutrophils**. When phagocytosis was induced in **neutrophils** by zymosan or bacteria, I was recovered in the medium together with other constituents of the specific granules, such as alkaline phosphatase and lysozyme. I extracted from leukocytes was able to bind the amount of Fe corresponding to its theoretical Fe-binding capacity. After injection of endotoxin into rats, I was detected in various tissues where it was normally absent, or in the plasma when the reticuloendothelial system (RES) had previously been blocked by India ink or aggregated **albumin**. Significant exchange of Fe from transferrin to I was observed in vitro only at a pH < 7.0 or in the presence of a high concentration of citrate. However, the fast elimination of I in vivo, when saturated with Fe, might account for the observed transfer of iron to endogenous or administered **apolactoferrin** (II). I.v. injection of human II into rats caused a marked decrease of the plasma Fe level. The kinetics of this process ruled out the possibility of a secondary **inflammatory** effect due to phlogogenic contaminants. By immunofluorescence, I was shown to be bound and **ingested** by monocytes. The rate of elimination of human Fe-I injected into rats was especially fast when compared to that of human II,

succinylated Fe-I, or other human proteins. Blockade of the RES slowed down the rate of clearance of Fe-I and also retarded the elimination of endogenous rat I released by endotoxin. Thus, specific receptors for Fe-I may exist on macrophage membranes.

```
=> s allevia? and  (l21 or l42 or l50)
L59             0 FILE MEDLINE
L60             1 FILE HCAPLUS
L61             0 FILE BIOSIS
L62             0 FILE EMBASE
L63             0 FILE JICST-EPLUS
L64             1 FILE WPIDS

TOTAL FOR ALL FILES
L65             2 ALLEVIA? AND (L21 OR L42 OR L50)

=> dup rem l65
PROCESSING COMPLETED FOR L65
L66             1 DUP REM L65 (1 DUPLICATE REMOVED)

=> d cbib abs

L66  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 1
2002:616360   Document No. 137:150231  Alleviating
     inflammation symptoms by administering a compn. contg.
     human-type lactoferrin.  Yajima, Masako; Nakayama,
     Makiko; Tsukamoto, Yumi; Koide, Kaoru; Kuwata, Tamotsu; Yajima, Takaji
     (Meiji Dairies Corporation, Japan).  U.S. Pat. Appl. Publ. US 2002111295
     A1 20020815, 13 pp.  (English).  CODEN: USXXCO.  APPLICATION: US
     2002-73297 20020213.  PRIORITY: JP 2001-38486 20010215.
AB   The invention provides agents for alleviating symptoms resulting
     from inflammation, which have an activity to alleviate
     inflammatory symptoms caused by bacterial infection, particularly
     accumulation of body fluid such as bronchocavernous
     plasma exudation, ascites, etc., at the inflammatory site, or
     excessive increase of blood neutrophils; symptoms resulting from
     inflammation caused by bacterial infection, particularly
     accumulation of body fluid such as bronchocavernous
     plasma exudation ascites, etc., at the inflammatory site, or
     excessive increase of blood neutrophils, can be
     alleviated effectively by infesting or administering
     orally or parenterally a composition containing human-type
     lactoferrin as an effective component.


=> s allevia? and inflam? and (bacterial infect? or bronchocaver? plasma exudat? or
plasma exudat? or ascite? or blood neutrophil?) and (oral? or parent? or ingest?)
and (lactoferrin or lactotransferrin)
L67             0 FILE MEDLINE
L68             1 FILE HCAPLUS
L69             0 FILE BIOSIS
L70             0 FILE EMBASE
L71             0 FILE JICST-EPLUS
L72             1 FILE WPIDS

TOTAL FOR ALL FILES
L73             2 ALLEVIA? AND INFLAM? AND (BACTERIAL INFECT? OR BRONCHOCAVER?
                  PLASMA EXUDAT? OR PLASMA EXUDAT? OR ASCITE? OR BLOOD NEUTROPHIL?
                  ) AND (ORAL? OR PARENT? OR INGEST?) AND (LACTOFERRIN OR LACTOTRA
                  NSFERRIN)
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Searched by: Mary Hale 571-272-2507 REM 1D86

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=> s l73 not l65
L74             0 FILE MEDLINE
L75             0 FILE HCAPLUS
L76             0 FILE BIOSIS
L77             0 FILE EMBASE
L78             0 FILE JICST-EPLUS
L79             0 FILE WPIDS

TOTAL FOR ALL FILES
L80             0 L73 NOT L65

=> s yajima, m?/au,in or yajima m?/au,in;s nakayama, m?/au,in or nakayama m?/au,in
'IN' IS NOT A VALID FIELD CODE
L81           176 FILE MEDLINE
L82           433 FILE HCAPLUS
L83           327 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L84           151 FILE EMBASE
L85           684 FILE JICST-EPLUS
L86            64 FILE WPIDS

TOTAL FOR ALL FILES
L87          1835 YAJIMA, M?/AU,IN OR YAJIMA M?/AU,IN


'IN' IS NOT A VALID FIELD CODE
L88          1055 FILE MEDLINE
L89          3071 FILE HCAPLUS
L90          1386 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L91           910 FILE EMBASE
L92          4025 FILE JICST-EPLUS
L93           478 FILE WPIDS

TOTAL FOR ALL FILES
L94         10925 NAKAYAMA, M?/AU,IN OR NAKAYAMA M?/AU,IN

=> s l87 and l94
L95             2 FILE MEDLINE
L96             3 FILE HCAPLUS
L97             3 FILE BIOSIS
L98             2 FILE EMBASE
L99             1 FILE JICST-EPLUS
L100            1 FILE WPIDS

TOTAL FOR ALL FILES
L101           12 L87 AND L94

=> s l101 and (tsukamoto, y? or tsukamoto y?)/au,in
'IN' IS NOT A VALID FIELD CODE
L102            0 FILE MEDLINE
L103            1 FILE HCAPLUS
L104            0 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L105            0 FILE EMBASE
L106            0 FILE JICST-EPLUS
L107            1 FILE WPIDS

TOTAL FOR ALL FILES
L108            2 L101 AND (TSUKAMOTO, Y? OR TSUKAMOTO Y?)/AU,IN

=> s l108 not l74
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Searched by: Mary Hale 571-272-2507 REM 1D86

<------User Break------>

SEARCH ENDED BY USER
SEARCH ENDED BY USER

=> s l108 not l73
L110 0 FILE MEDLINE
L111 0 FILE HCAPLUS
L112 0 FILE BIOSIS
L113 0 FILE EMBASE
L114 0 FILE JICST-EPLUS
L115 0 FILE WPIDS

TOTAL FOR ALL FILES
L116 0 L108 NOT L73

=> log y

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